NEW STRATEGIES FOR THE TOTAL SYNTHESIS OF AZA-PROPELLANE NATURAL PRODUCTS

Thesis by

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To my family

ACKNOWLEDGEMENTS

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have experienced a number of ups and downs together, and I couldn't have asked for a better group of friends to do so with.

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ABSTRACT

The propellane alkaloids comprise a large class of natural products that possess varying degrees of structural complexity and biological activity. The earliest of these to be isolated was acutumine, a chlorinated alkaloid that has been shown to exhibit selective T-cell cytotoxicity and antiamnesic properties. Alternatively, the hasubanan family of natural products has garnered considerable attention from the synthetic community in part due to its structural similarities to morphine. While these alkaloids have been the subject of numerous synthetic studies over the last forty years, very few enantioselective total syntheses have been reported to date.

As part of a research program directed towards the synthesis of various alkaloid natural products, we have developed a unified strategy for the preparation of the hasubanan and acutumine alkaloids. Specifically, a highly diastereoselective 1,2-addition of organometallic reagents to benzoquinone-derived *tert*-butanesulfinimines was established, which provides access to enantioenriched 4-aminocyclohexadienone products. This methodology enabled the enantioselective construction of functionalized dihydroindolones, which were found to undergo intramolecular Friedel-Crafts conjugate additions to furnish the propellane cores of several hasubanan alkaloids. As a result of these studies, the first enantioselective total syntheses of 8-demethoxyrunanine and cepharatines A, C, and D were accomplished in 9-11 steps from commercially available starting materials.

More recent efforts have focused on applying the sulfinimine methodology to the synthesis of a more structurally complex propellane alkaloid, acutumine. Extensive studies have determined that a properly functionalized dihydroindolone undergoes a

photochemical [2+2] cycloaddition followed by a lactone fragmentation/Dieckmann cyclization to establish the carbocyclic framework of the natural product. The preparation of more appropriately oxidized propellane intermediates is currently under investigation, and is anticipated to facilitate our synthetic endeavors toward acutumine.

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LIST OF ABBREVIATIONS

$[\alpha]_D$	angle of optical rotation of plane-polarized light
Å	angstrom(s)
Ac	acetyl
AIBN	azobisisobutyronitrile
app	apparent
aq	aqueous
Ar	aryl group
atm	atmosphere(s)
Bn	benzyl
Boc	*tert*-butoxycarbonyl
bp	boiling point
br	broad
Bu	butyl
n-Bu	butyl or *norm*-butyl
t-Bu	*tert*-butyl
c	concentration of sample for measurement of optical rotation
^{13}C	carbon-13 isotope
^{14}C	carbon-14 isotope
/C	supported on activated carbon charcoal
°C	degrees Celcius
calc'd	calculated
CBS	Corey-Bakshi-Shibata

Cbz	benzyloxycarbonyl
cm^{-1}	wavenumber(s)
CN	nitrile
conc.	concentrated
Cy	cyclohexyl
d	doublet
d	dextrorotatory
D	deuterium
dba	dibenzylideneacetone
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DHP	dihydropyran
DIBAL	diisobutylaluminum hydride
DMAP	4-dimethylaminopyridine
DME	1,2-dimethoxyethane
DMF	*N*,*N*-dimethylformamide
DMP	Dess–Martin periodinane
DMSO	dimethylsulfoxide
dppp	1,3-bis(diphenylphosphino)propane
dr	diastereomeric ratio
ee	enantiomeric excess
E^+	electrophile
E	trans (entgegen) olefin geometry
EDC	*N*-ethyl-*N*'-(3-dimethylaminopropyl)carbodiimide

e.g.	for example (Latin: *exempli gratia*)
eq	equation
ESI	electrospray ionization
Et	ethyl
et al.	and others (Latin: *et alii*)
FAB	fast atom bombardment
g	gram(s)
h	hour(s)
^{1}H	proton
^{2}H	deuterium
^{3}H	tritium
H-G II	Hoveyda-Grubbs, 2nd generation
HMDS	hexamethyldisilamide or hexamethyldisilazide
HMPA	hexamethylphosphoramide
$h\nu$	light
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrometry
Hz	hertz
i.e.	that is (Latin: *id est*)
IR	infrared spectroscopy
J	coupling constant
k	rate constant
kcal	kilocalorie(s)

kg	kilogram(s)
L	liter or neutral ligand
l	levorotatory
LA	Lewis acid
LAH	lithium aluminum hydride
LDA	lithium diisopropylamide
m	multiplet or meter(s)
M	molar or molecular ion
m	meta
μ	micro
m-CPBA	*meta*-chloroperbenzoic acid
Me	methyl
mg	milligram(s)
MHz	megahertz
min	minute(s)
mL	milliliter(s)
mol	mole(s)
MOM	methoxymethyl
mp	melting point
Ms	methanesulfonyl (mesyl)
m/*z*	mass-to-charge ratio
N	normal or molar
NBS	*N*-bromosuccinimide

NIS	*N*-iodosuccinimide
nm	nanometer(s)
NMO	*N*-methylmorpholine-*N*-oxide
NMR	nuclear magnetic resonance
NOE	nuclear Overhauser effect
NOESY	nuclear Overhauser enhancement spectroscopy
Nu^-	nucleophile
o	ortho
p	para
Ph	phenyl
pH	hydrogen ion concentration in aqueous solution
pK_a	acid dissociation constant
PMB	*para*-methoxybenzyl
PMHS	polymethylhydrosiloxane
ppm	parts per million
Pr	propyl
i-Pr	isopropyl
n-Pr	propyl or *norm*-propyl
psi	pounds per square inch
pyr	pyridine
q	quartet
R	alkyl group
R	rectus

ref	reference
R_f	retention factor
s	singlet or seconds
S	sinister
t	triplet
TBAF	tetra-*n*-butylammonium fluoride
TBHP	*tert*-butyl hydroperoxide
TBS	*tert*-butyldimethylsilyl
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
TFAA	trifluoracetic anhydride
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
TMSE	2-(trimethylsilyl)ethyl
TOF	time-of-flight
tol	tolyl
Ts	*para*-toluenesulfonyl (tosyl)
UV	ultraviolet
w/v	weight per volume
v/v	volume per volume
X	anionic ligand or halide
Z	cis (zusammen) olefin geometry

CHAPTER 1

An Introduction to the Hasubanan Alkaloids

1.1. Introduction

The hasubanan alkaloids comprise a large class of natural products isolated from the Menispermaceae family of plants, which have long been used in traditional Chinese medicine for the treatment of pain, arthritis, fever, and many other illnesses.[1] Since their initial discovery in the 1920s, over 80 members of this collection of alkaloids have been isolated to date.[1,2] Each of these compounds can be structurally characterized by the presence of a densely functionalized [4.4.3] propellane framework (**3**, Figure 1); and can be further organized based on the oxidation pattern that adorns their propellane core. For example, cepharamine (**1**) and 8-demethoxyrunanine (**2**) constitute the least oxidized hasubanan alkaloids, due to their lack of a functional group at the C8 carbon. Introduction of a C8 oxygen functionality leads to natural products bearing the hasubanonine oxidation pattern, such as hasubanonine (**4**), aknadinine (**5**), runanine (**6**), and delavayine (**7**). Additional oxidation at the C10 carbon is characteristic of the oxo-bridged propellane

alkaloids, including metaphanine (**8**), longanine (**9**), periglaucine A (**10**), and stephabenine (**11**).

Since their initial structural elucidation in the 1960s, the hasubanan alkaloids have garnered considerable attention from the synthetic community in part due to their resemblance to morphine. Indeed, the hasubanan and morphinan frameworks differ primarily in their D ring composition: whereas **3** contains a C14-N bond to form a pyrrolidine, the morphine backbone presents the analogous C9-N-linked piperidine ring. Additionally, these natural products are of opposite enantiomeric series; as a result, it has been speculated that the unnatural enantiomers of the hasubanan alkaloids might exhibit analgesic activity.[1] Although studies aimed at assessing this hypothesis have yet to be reported, several naturally occurring hasubanans display promising biological properties. For instance, the oxo-bridged propellanes periglaucine A (**10**) and longanine (**9**) were found to demonstrate anti-hepatitis B virus activity and selective δ-opioid receptor binding affinity, respectively.[3]

As a result of their unique molecular architecture and potential biological applications, the hasubanans have been the subject of numerous synthetic endeavors over the last 50 years. Herein, the diverse array of strategies employed to target their propellane framework are discussed. Preceding the discussion of these reports, a brief history of the hasubanan family of natural products is presented, including their isolation and biosynthetic origins.

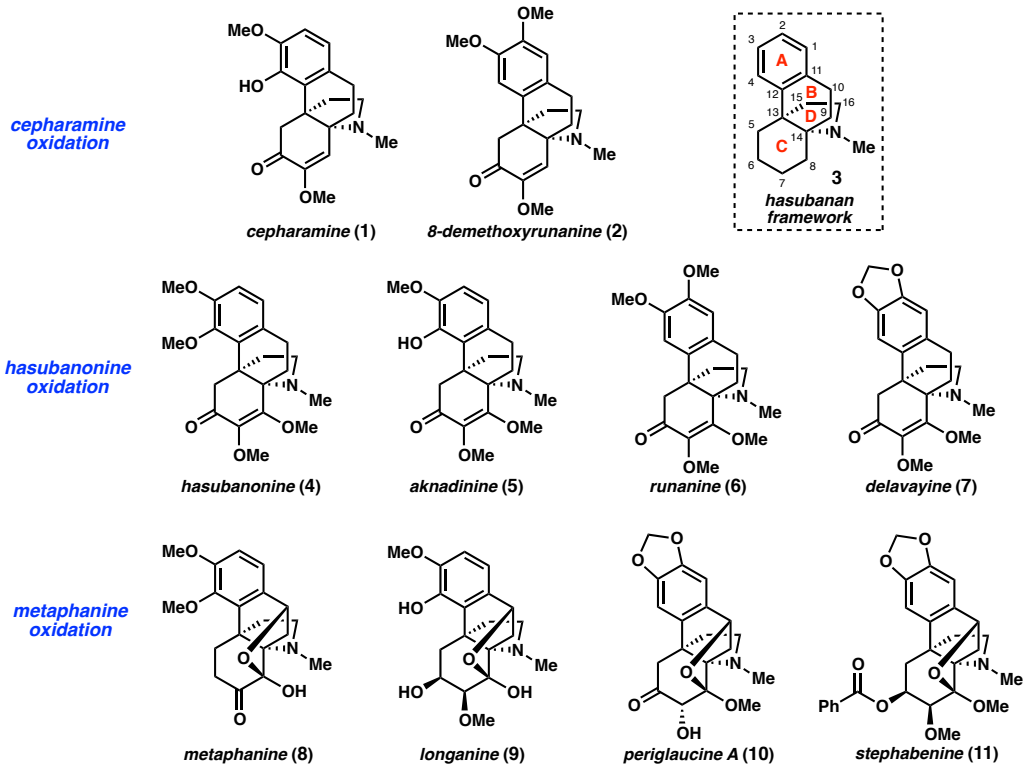

Figure 1. Representative members of the hasubanan alkaloids.

1.2. Isolation

In 1924, Kondo and coworkers described the isolation of metaphanine (**8**), an oxo-bridged hasubanan alkaloid.[4] Its structure was not elucidated until 1964, when Takeda and coworkers characterized the new compound by IR and 1D NMR spectroscopy, as well as a number of derivitazation studies.[5] Specifically, degradation of **8** under reducing conditions delivered anthracene derivative **12**, a structural motif observed to arise from the degradation of morphine alkaloids (Figure 2). In addition, sequential reduction of **8** afforded hasubanan **13**, a known compound whose enantiomer has been prepared from a codeinone intermediate. Using these structural techniques, Tomita and coworkers disclosed the structures of cepharamine (**1**)[6] and hasubanonine (**4**).[7] These structural

assignments were validated in 1968, when Kupchan and coworkers obtained an X-ray crystal structure of the brosylate derivative of aknadinine (**5**).[8] As novel hasubanan alkaloids began to emerge, 2D NMR techniques and mass spectrometry became important tools for more efficient structural determination. For example, the structure of runanine (**6**) was ascertained by extensive NOE experiments. Additionally, the most abundant ion peak observed in the mass spectrum of **6** was m/z = 315, which corresponds to loss of its ethylamine chain.[9] This type of fragmentation is characteristic of propellane alkaloids bearing the hasubanonine framework.[10] Taken together, these pioneering studies laid the foundation for the characterization of subsequently discovered hasubanan alkaloids.

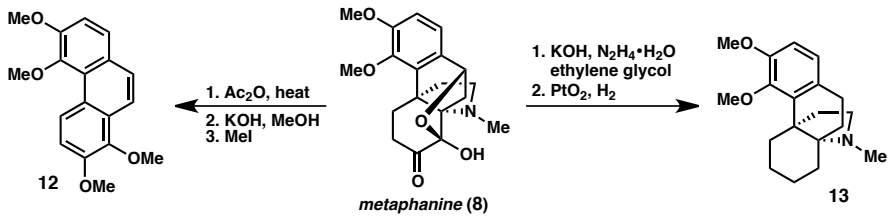

Figure 2. Structural elucidation of metaphanine (**8**).

In more recent years, a significant number of natural products comprising the metaphanine oxidation pattern have been discovered: over 20 oxo-bridged hasubanans have been reported in the last 10 years.[11] Interestingly, members of this subfamily of alkaloids are the only hasubanans found to demonstrate medicinal properties (*vide supra*). Moreover, the recent emergence of oxo-bridged hasubanans in the literature raises numerous questions regarding their biosynthetic relationship to their less oxidized congeners. While studies that probe the biological relationship of these alkaloids are

limited, elegant studies that shed light on their biosynthesis have been conducted and are presented below.

1.3. Biosynthesis

The structural similarities between the morphinan and hasubanan alkaloids have been exploited to examine the biosynthesis of hasubanonine. Specifically, it is known that morphine is derived from the coupling of two tyrosine building blocks, which initially generates an isoquinoline intermediate.[12] With these considerations in mind, Battersby and coworkers conducted feeding experiments with ^{14}C-labeled tyrosine and isoquinoline derivatives bearing an array of arene oxidation patterns.[13] These investigations revealed that the hasubanan framework is indeed derived from two different tyrosine-based building blocks. Moreover, the authors concluded that the C ring of **5** originates from trioxygenated intermediate **14** (Figure 3). Importantly, the oxidation of tyrosine occurs prior to isoquinoline formation: a number of analogous mono- and dioxygenated isoquinolines were not incorporated into the natural product.

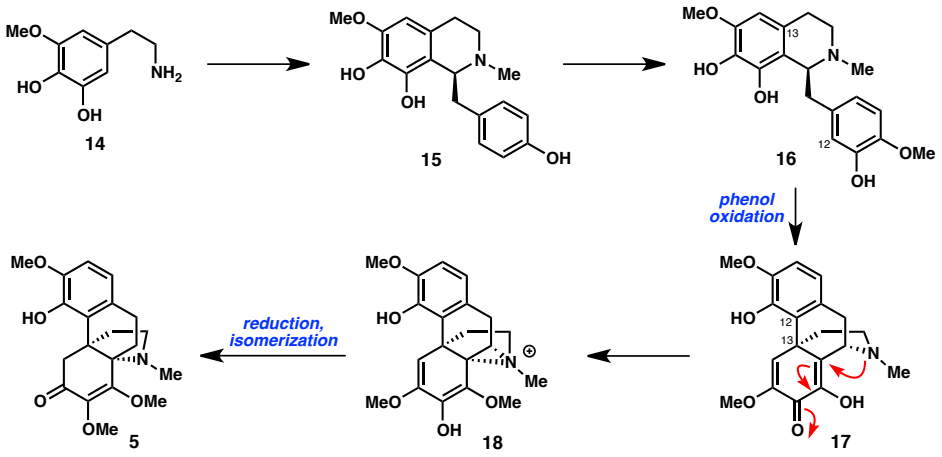

Figure 3. Proposed biosynthesis of the hasubanan alkaloids.

Based on these findings, **14** is believed to undergo a condensation reaction with a tyrosine derivative to deliver **15**, which upon oxidation affords **16**.[10] In analogy to morphinan biosynthesis, an intramolecular oxidative coupling between the C12-C13 carbons is believed to deliver piperidine **17**. At this point, the propellane backbone is hypothesized to arise from an initial intramolecular conjugate addition of the basic amine into the enone system, giving rise to aziridinium ion **18**. Reduction of this intermediate generates the corresponding pyrrolidine, which can then undergo isomerization of the C ring to give **5**.

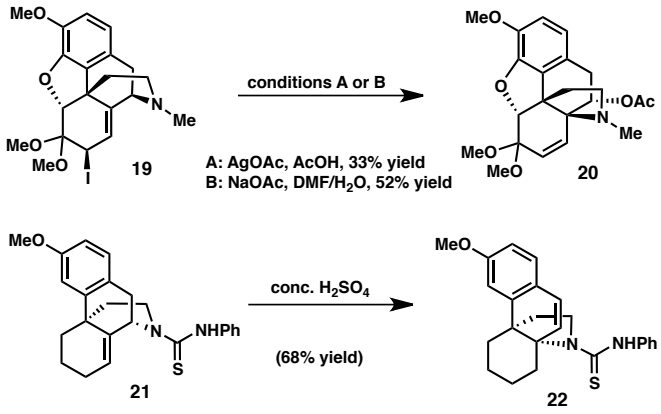

Figure 4. Conversion of morphinans to propellane intermediates.

Although the proposed skeletal rearrangement of **17** to **5** has not been validated with experimental data, researchers have successfully converted a morphine derivative to a propellane alkaloid. In one example, Kirby and coworkers facilitated the conversion of thebaine-derived iodide **19** to propellane **20** by exposure to Ag- or NaOAc (Figure 4);[14] this reaction presumably proceeds via displacement of the allylic iodide. In a similar transformation, treatment of morphinan **21** with concentrated H_2SO_4 gives pyrrolidine **22**

in 68% yield.[15] While these examples remain limited, they provide credence for the biosynthetic relationship between the hasubanan and morphinan family of alkaloids.

1.4. Previous Synthetic Studies

Over the last five decades, the hasubanan alkaloids have been the subject of numerous synthetic studies. While a number of racemic syntheses of the hasubanan core have been described, there exist few reports that details their enantioselective total synthesis. Nevertheless, these collective studies highlight the diverse array of strategies that can be implemented to prepare the hasubanan framework. The discussion below is intended to highlight the key features of these synthetic endeavors, and is divided into two sections: core syntheses and total syntheses.

1.4.1. Core Syntheses

Of the existing synthetic studies toward the hasubanan framework, the most common relies on a late-stage intramolecular aminocyclization reaction to establish the D ring of the natural product (see **3**, Figure 1). The earliest example of this strategy was presented by Ibuka and Kitano in 1966.[16] Benzylic oxidation of sinomenine-derived alkaloid **23** gave ketone **24** after protecting group manipulations (Figure 5). Reductive cleavage of the C9-N bond of **24** with zinc dust, followed by exposure to bromine, provided the corresponding α-bromo ketone. Exposure of the bromide to LiCl and Li_2CO_3 in DMF at 120 °C promoted the formation of enone **25**, which spontaneously undergoes cyclization by the pendant amine to yield propellane **26**, albeit in poor yield.

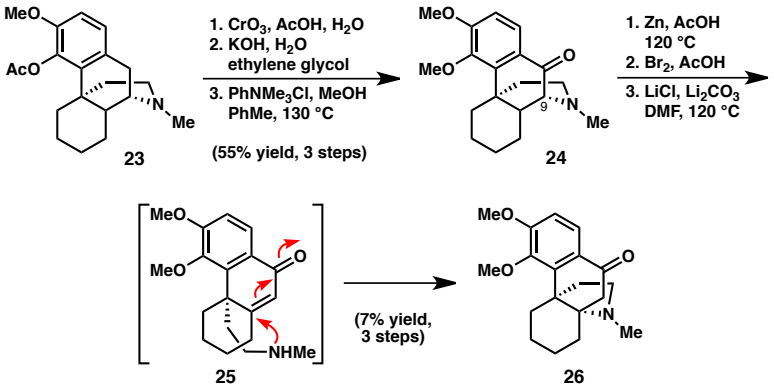

Figure 5. Synthesis of **26** from a sinomenine derivative.

In their efforts to prepare more effective morphine analgesics, the Bristol Myers group reported the synthesis of a number of morphinan and hasubanan derivatives. In the context of propellane alkaloids, the authors targeted the synthesis of amine **28** from α-tetralone-derived tricycle **27** (Figure 6).[17] Exposure of **27** to the lithium anion of MeCN afforded the cyanomethyl adduct, which could be reduced in situ with LAH to give the corresponding amino alcohol. Wagner-Meerwein rearrangement of this intermediate was effected under acidic conditions to yield amine **28** in 56% yield over two steps. At this point, an aminocyclization reaction was effected by treatment of **28** with bromine to generate the hydrobromide salt of propellane **29** in 72% yield. The authors were able to extend this aminocyclization protocol to an epoxide-bearing substrate, providing access to alcohol **30** in good yield. Concomitant to the studies by Bristol-Myers, Shiotani and Kometani reported the direct aminocyclization reaction of amine **28**.[18] In the event, propellane **31** was obtained in 90% yield by exposure of **28** to paraformaldehyde and formic acid. Presumably, cyclization of the pendant amine occurs via the intermediacy of a C14 carbocation, and the resulting pyrrolidine can then undergo an Eschweiler-Clark methylation.[19]

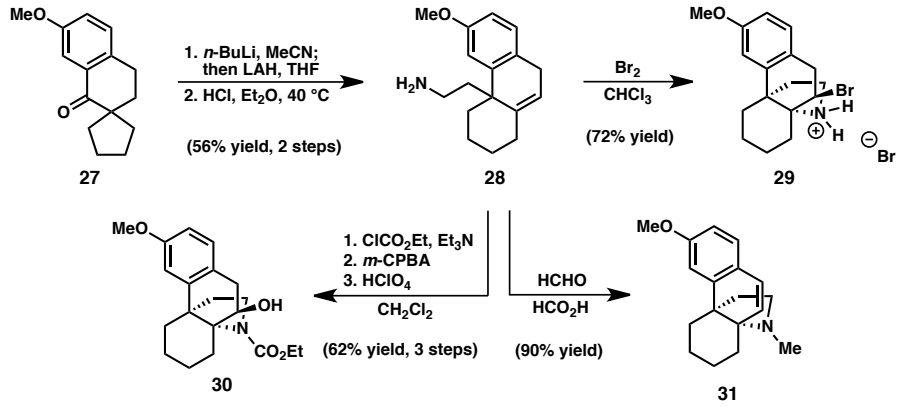

Figure 6. Bristol–Myers' and Kometani's aminocyclization approaches.

The most recent core synthesis involving an aminocyclization reaction stems from work by the Mulzer group. Their synthetic endeavors commenced with tricyclic enone **32**, which is available in 3 steps from commercially available 4-(3,4-dimethoxyphenyl)butyric acid (Figure 7).[20] Vinylcuprate addition to the enone yields olefin **33**, which in eight steps can be elaborated to azide **34**. To facilitate formation of the requisite pyrrolidine ring, a thermal (3+2) dipolar cycloaddition reaction of **34** was conducted to access triazene **35** in good yield. Decomposition of the triazene can then be achieved by heating **35** in refluxing pyridine to give propellane **36**.

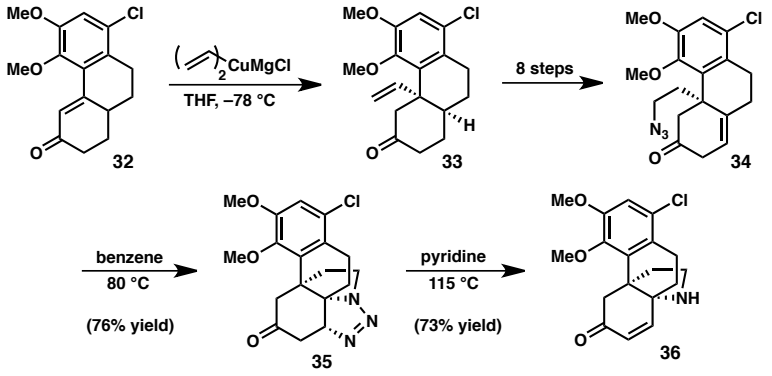

Figure 7. Mulzer's (3+2) cycloaddition approach to the propellane alkaloids.

Another approach for propellane synthesis exploits the reactivity of tetrahydrobenzindoles. In 1969, Evans and Tahk independently disclosed the Robinson annulation of enamine **38** with methyl vinyl ketone (Figure 8).[21,22] However, this reaction promotes the formation of **37** in only modest yield.[23] Evans observed in improvement in the yield of this reaction when methyl pentadienoate (**39**) was used as the electrophile, thereby furnishing **40** in 50% yield.[24]

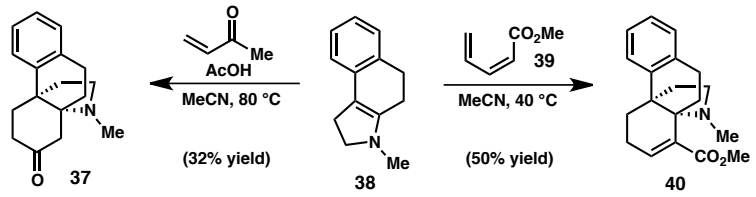

Figure 8. Preparation of the hasubanan core via enamine **38**.

The Hoffman-La Roche group devised an approach to the hasubanan framework starting from cyclohexanone derivative **41** (Figure 9).[25] Aldol reaction between **41** and ethyl acetate provided alcohol **42**, which was then subjected to $POCl_3$ in pyridine to yield a 2:1 mixture of α,β and β,γ-unsaturated esters. Treatment of this mixture of products with Raney-Ni, NH_3, and H_2 unveiled primary amine **43**, which adds into the conjugated enone to produce *cis*-fused pyrrolidine **44**. Installation of the B ring is accomplished by an acid-mediated Friedel-Crafts reaction of the arene with the ester moiety of **44**, providing tetracycle **45** in 83% yield.

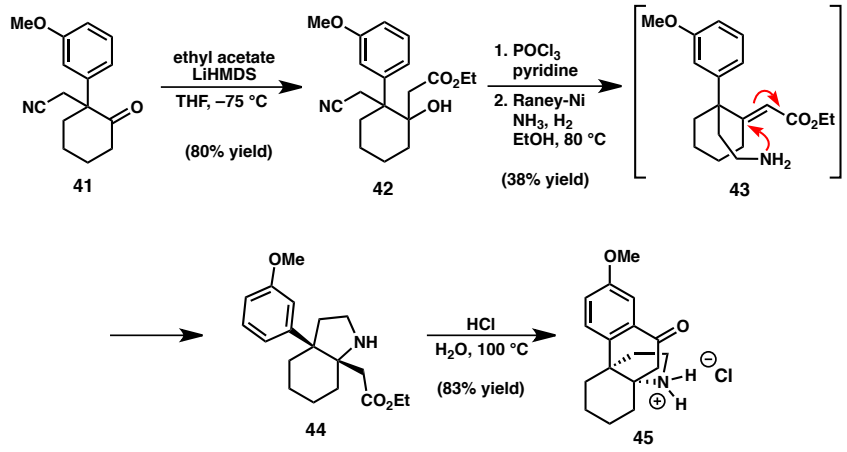

Figure 9. Synthesis of **45** from cyclohexanone **41**.

In contrast to the previously discussed core syntheses, the Kobayashi group pursued an approach that focused on a late-stage C-ring formation.[26] To this end, β–tetralone was readily converted to alcohol **46**, which upon Swern oxidation and cleavage of the Boc group generates unstable imine intermediate **47** (Figure 10). To circumvent decomposition of **47**, the crude product was immediately treated with KCN in AcOH and DMF to give the hydrocyanation product. The resulting amine was *N*-formylated with formic acetic anhydride to afford tricycle **48**. Reduction of the nitrile functionality to its methyl ester proved nontrivial; the authors accomplished this transformation in five steps from **48** via the intermediacy of an *N*-acylbenzotriazole. Permanganate oxidation of **49** followed by methylation generated ketone **50** in 87% yield. Completion of the propellane backbone was realized by a Dieckmann condensation reaction and methylation with $TMSCHN_2$; however, the desired alkaloid (**51**) was obtained as a 1:1 mixture with its enol tautomer (**52**). Unfortunately, attempts to convert the undesired regioisomer to **51** were unsuccessful.

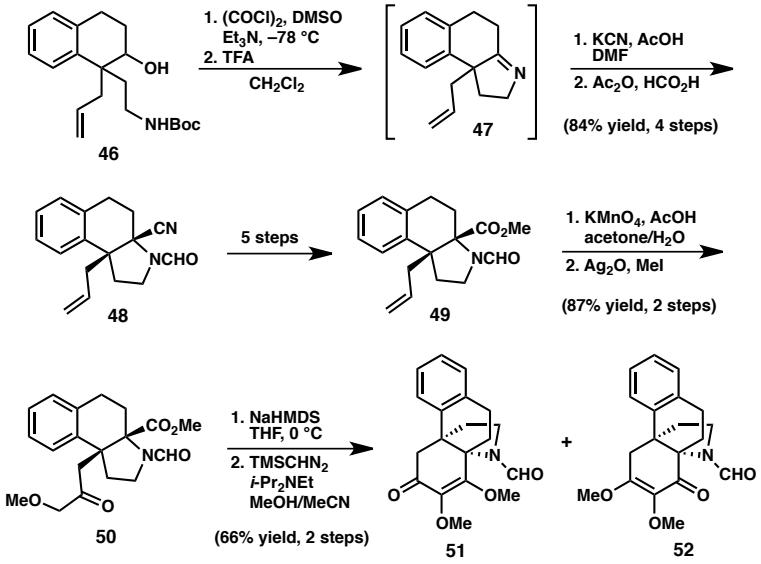

Figure 10. Kobayashi's synthesis of hasubanan congener **51**.

1.4.2. Total Syntheses

Shortly after the structure of hasubanonine was confirmed, Ibuka and coworkers embarked on a research campaign aimed at preparing a number of hasubanan alkaloids. Specifically, their synthetic strategy was highly dependent on the preparation and differential oxidation of propellane **56** (Figure 11). Beginning with tetralone derivative **53**, an interrupted Robinson annulation with methyl vinyl ketone furnished bridged ketone **54**.[27,28] Exposure of this intermediate to NaOEt in EtOH facilitated a retro-aldol/aldol reaction followed by a nitrile hydrolysis/conjugate addition cascade to give **55** in 50% yield over two steps. Further functional group manipulations allowed access to differentially protected phenol **56**.

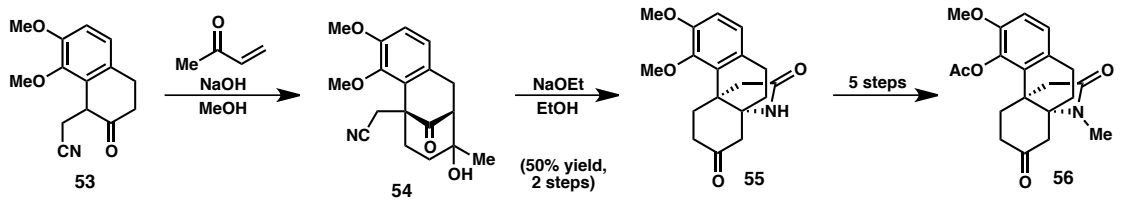

Figure 11. Ibuka's synthesis of tetracycle **56**.

With **56** in hand, the authors initially pursued a synthesis of cepharamine (**1**, Figure 12). Methoxy enone **57** was prepared from **56** via oxidation to the diketone followed by methylation with BF_3•OEt_2 in MeOH. Global reduction of the carbonyl moieties with LAH and subsequent oxidation of the resulting allylic alcohol delivered the natural product (**1**) in low yield.[28] Alternatively, **56** could be elaborated to the hasubanonine oxidation pattern by an initial α-acetoxylation to give **58**.[29,30] A series of oxidative manipulations provided diketone **59**, an intermediate that was treated with diazomethane to give aknadilactam (**60**)[31] and **61** in 8 and 23% yield, respectively. In this methylation reaction, the authors observe the formation of **60**, **61**, and each of their corresponding enol ether regioisomers in a 1:1:1:1 ratio, which accounts for the low isolated yields. Reduction of lactam **61** was effected by LAH reduction and MnO_2 oxidation to afford hasubanonine (**4**).

As a testament to the divergent nature of Ibuka's strategy, acetate **58** was also advanced to metaphanine (**8**). In this case, benzylic ketone **62** could be prepared from **58** after a series of steps including benzylic oxidation.[32,33] After an exhaustive screen of reducing conditions, the authors found reduction of the ketone with Al(O*i*-Pr)$_3$ in PhMe/*i*-PrOH to be optimal, delivering the corresponding alcohol in good yield and excellent diastereoselectivity (>20:1). Protection of the benzylic alcohol as its THP ether and

oxidation of the C8 alcohol provides the corresponding ketone, which spontaneously undergoes intramolecular ketalization after deprotection of the THP group to furnish oxo-bridged compound **63**. To complete the synthesis, the amide functionality of **63** was reduced utilizing Meerwein's salt and $NaBH_4$, and the ketal was hydrolyzed under acidic conditions.

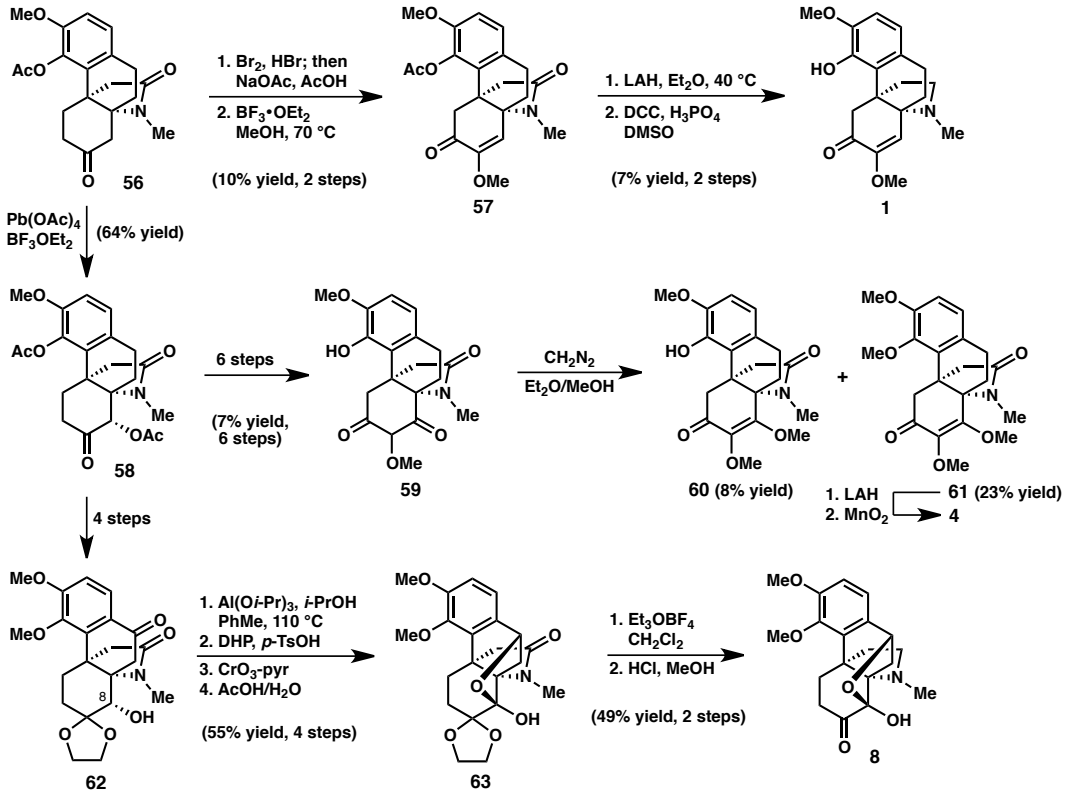

Figure 12. Ibuka's syntheses of hasubanan alkaloids.

Soon after the publication of Ibuka's studies, Kametani and coworkers reported their efforts toward capharamine (**1**, Figure 13).[34] In this biomimetic approach, the authors sought to construct the hasubanan backbone from simple isoquinoline precursors. To this end, reticuline-derived isoquinoline **64** was sequentially subjected to TFAA and Adam's

catalyst to access intermediate **65**. In the key step in their synthesis, photoexcitation of **65** with a mercury lamp promoted an intramolecular biaryl coupling to afford dienone **66**. Hydrolysis of the trifluoroacetamide group under basic conditions facilitated cyclization of the amine into the more electron poor enone to selectively give tetracycle **67**. Acid-mediated isomerization of the methoxyenone then delivered the natural product (**1**). More recently, Schwartz and Wallace described the direct oxidative coupling of **68** in the presence of thallium (III) trifluoroacetate, thereby completing a formal synthesis of cepharamine.[35]

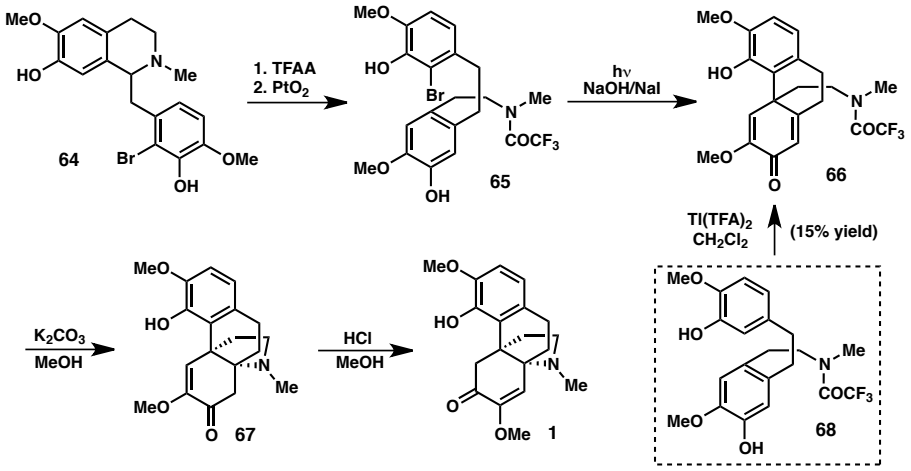

Figure 13. Kametani's preparation of cepharamine (**1**).

The synthetic endeavors of Ibuka and Kametani represented the sole completed syntheses of the hasubanans for over 20 years. Indeed, the subsequent total synthesis of a propellane alkaloid was not reported until 1998, when Schultz and Wang disclosed their preparation of (+)-cepharamine.[36] Starting with chiral benzamide **69**, Birch reduction followed by in situ alkylation with alkyl iodide **70** provided cyclohexadiene **71** in

excellent yield and as a single diastereomer (Figure 14). In an additional 6 steps, the authors could access lactone **72**. Exposure of **72** to AIBN and Bu_3SnH in refluxing benzene facilitated an intramolecular radical cyclization, thereby delivering hydrophenanthrene **73** after a few protecting group manipulations in 55% yield over 3 steps. Introduction of the amine was effected under a Hoffman rearrangement to give carbamate **74**, which upon LAH reduction unveils amide **75** and undergoes cyclization to furnish propellane **76**. Finally, oxidation of the alcohol, methyl enol ether formation, and ketal hydrolysis yielded the unnatural antipode of the natural product (**1**). With a longest linear sequence of 21 steps, this represents the first enantioselective preparation of any member of the hasubanan alkaloids.

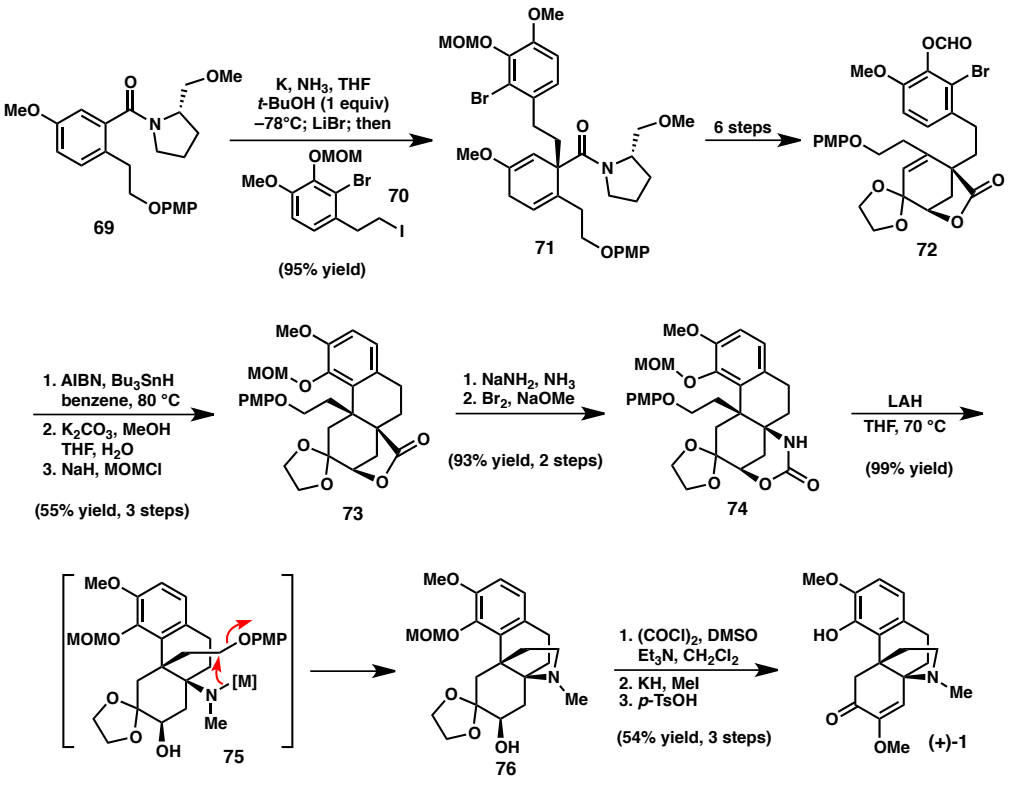

Figure 14. Schultz's enantioselective synthesis of (+)-cepharamine (**1**).

In 2011, Herzon and coworkers reported the development of a unified strategy for the enantioselective synthesis of several hasubanan alkaloids.[37] In contrast to Schultz's report, this synthetic approach relied on the enantioselective installation of the C14 stereocenter. To achieve this, an oxazaborolidine-catalyzed Diels-Alder reaction between quinone **77** and cyclopentadiene **78** afforded enedione **80** in 78% yield and 93% ee (Figure 15). Staudinger reduction of **80** then generated the corresponding quinone imine, which was activated toward nucleophilic attack by treatment with methyl triflate to give iminium salt **81**. Addition of an alkynyl lithium reagent (e.g., **82**) then gives pyrrolidine **83** in good yield. Using this 1,2-addition strategy, the authors can access an array of hasubanan frameworks by modifying the nature of the alkynyllithium nucleophile employed.

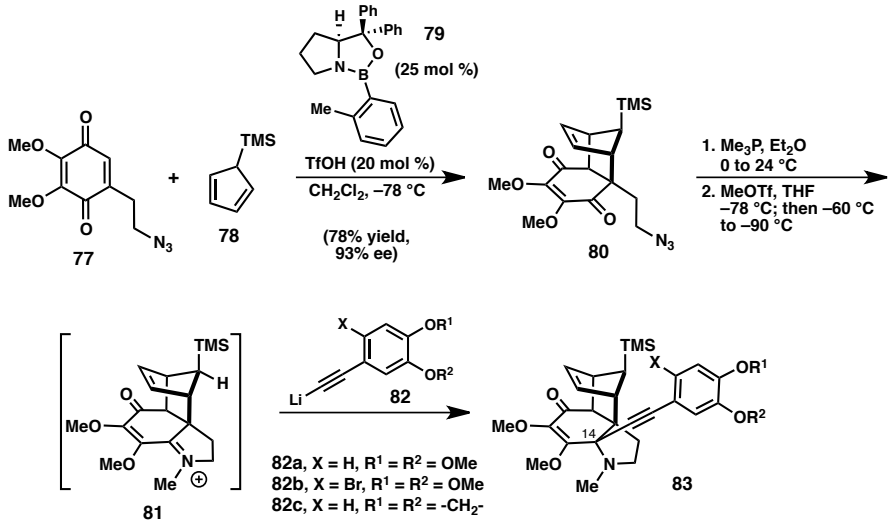

Figure 15. Herzon's general approach to the hasubanans.

To prepare (–)-runanine (**6**), addition of **82a** to iminium **81** afforded **83a** in 93% yield (Figure 16). Thermolysis of the cyclopentenyl group and monoreduction of the alkyne

with Crabtree's catalyst provides dienone **85**, an intermediate found to undergo a triflic acid-mediated intramolecular conjugate addition to give the propellane core. Finally, hydrogenation of the resulting olefin with Wilkinson's catalyst generates **6**. Using a similar reaction sequence, the authors could also access (–)-hasubanonine (**4**) and (–)-delavayine (**7**). Alternatively, hydration of alkene **89** with $Co(acac)_2$ under an atmosphere of oxygen followed by addition of formic acid gave periglaucine B (**90**) in 55% yield.

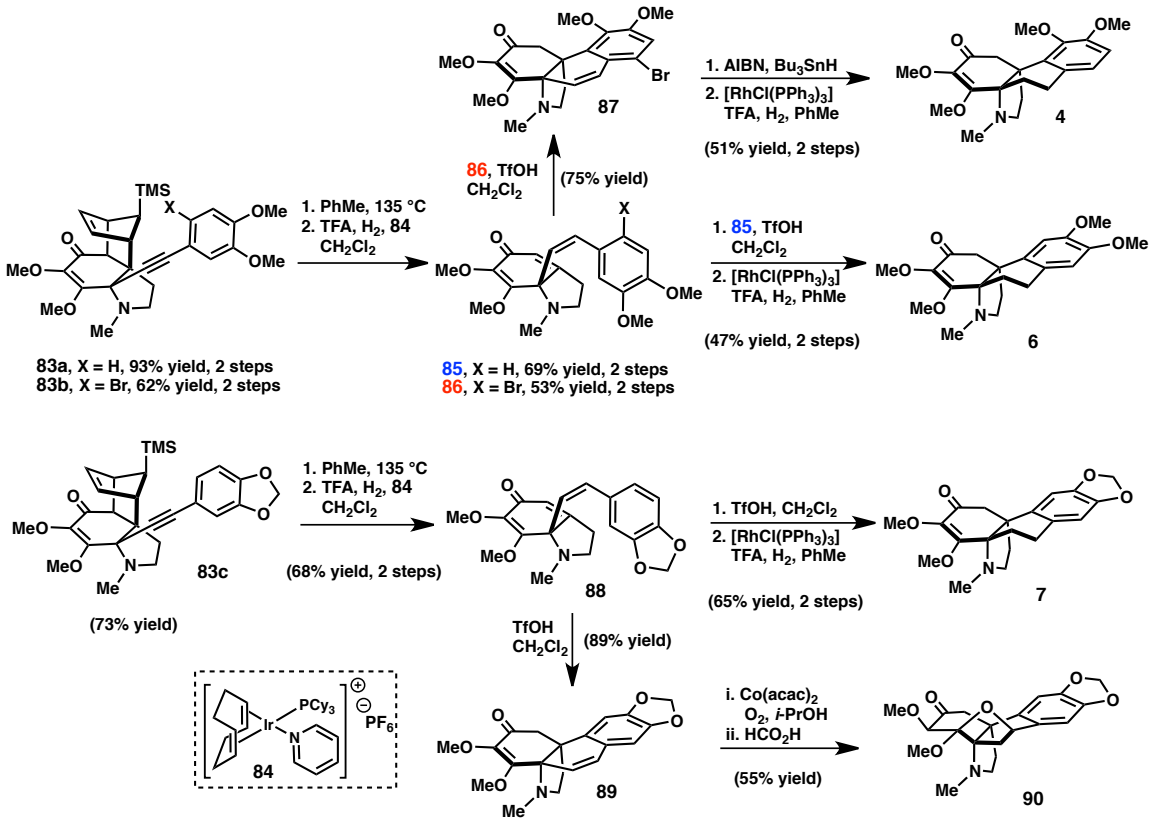

Figure 16. Herzon's synthesis of hasubanan alkaloids.

1.5. Concluding Remarks

Today, the hasubanan alkaloids remain an important family of biologically relevant natural products. Indeed, as the number of new hasubanans continue to grow, so too does

chemists' interest in their biological properties and structural complexity. The studies discussed above serve as a testament to this growing interest: a number of elegant approaches that target the hasubanan core have been developed, and enantioselective syntheses of their unique molecular architecture have begun to emerge. The further development of new, enantioselective approaches to the hasubanans will ultimately allow researchers to further characterize their biological properties, as well as contribute novel reactions for complex molecule synthesis.

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CHAPTER 2

Development of a Diastereoselective 1,2-Addition to Sulfinyl Imines: Application to the Hasubanan Alkaloids[†]

2.1. Introduction

As was illustrated in the previous chapter, the hasubanan alkaloids remain elusive targets for *enantioselective* total synthesis. While their structure comprises a relatively compact, tetracyclic framework, their azapropellane core presents several notable challenges. First, this backbone is structurally defined by a central pair of fully-substituted carbon stereocenters, a motif difficult to access using modern synthetic methods. In addition, the different oxidation patterns that decorate the propellane core introduce variable functionality that can (1) enhance its sterically congested nature, and (2) significantly alter their relative reactivity. The following chapter details our own

[†] Portions of this chapter have been reproduced from published studies (see references 1 and 2) and the supporting information found therein. The research presented in this chapter was completed in collaboration with Kangway V. Chuang, a graduate student in the Reisman group.

efforts toward these alkaloids,[1,2] which have culminated in the efficient enantioselective preparation of several hasubanans.

2.2. Synthetic Approach

2.2.1. Retrosynthetic Analysis. As part of a research program directed towards the synthesis of various alkaloid natural products, we sought to develop a unified strategy for the preparation of several hasubanan alkaloids (Figure 1). More specifically, it was hypothesized that the propellane core of **2**, **4**, and **10** could be readily accessed from an appropriately functionalized dihydroindolone (e.g., **91**) via late-stage introduction of the appropriate peripheral oxidation. The dihydroindolone was anticipated to derive from 4-aminocyclohexadienone **92**, the product of a diastereoselective 1,2-addition of an organometallic nucleophile to a quinone-derived sulfinyl imine (e.g., **93**). Although Swenton and coworkers utilized an intermediate akin to **92** in their synthetic studies toward the erythrina alkaloids, the *enantioselective* preparation of such compounds has not been fully explored.[3] Notably, by varying the identity of the nucleophile, several members of the hasubanan family could be readily accessed.

While attractive from a strategic standpoint, it was recognized that the proposed synthesis presented several challenges. Its successful application to the total synthesis of the hasubanans would require (1) the development of a 1,2-addition reaction to quinone-derived imines *with control over the absolute configuration about the C14-N bond*, and (2) the utilization of a nitrogen protecting group that would prevent any deleterious dienone-phenol rearrangements.[4] Despite numerous reports targeting the preparation enantioenriched chiral amines, the asymmetric synthesis of α,α-disubstituted amines by

nucleophilic 1,2-addition to ketimines—and specifically, benzoquinone-derived imines—remains an underdeveloped arena in organic synthesis.[5,6] Moreover, current *catalytic, asymmetric* syntheses of these structural motifs are limited by the scope of the nucleophile or the *N*-protecting group employed.[7]

With these considerations in mind, it was envisioned that benzoquinone imines derived from *N*-*tert*-butanesulfinamide should fulfill the abovementioned criteria. Pioneering work by Ellman and coworkers has demonstrated that *N*-*tert*-butanesulfinyl aldimines and ketimines undergo nucleophilic additions of organolithium and organomagnesium reagents to furnish *N*-sulfinamides with high diastereoselectivity.[8] Further, in the context of sulfinamide **92,** the electron withdrawing nature of the *N*-sulfinyl group was expected to disfavor any potential dienone-phenol rearrangements. Detailed below are our preliminary studies that demonstrate the feasibility of this approach for the synthesis of hasubanan alkaloids.

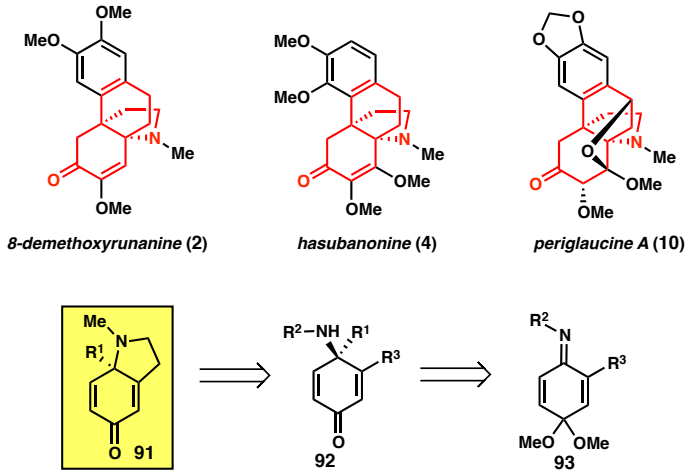


Figure 1. Representative hasubanan alkaloids and proposed strategy.

2.2.2. Development of a Diastereoselective 1,2-Addition to Benzoquinone-Derived t-Butanesulfinimines. At the outset of our studies, we sought to evaluate conditions for the synthesis of benzoquinone-derived sulfinimines (e.g., **96**, Figure 2). Studies by Ellman and coworkers have shown that *N*-sulfinyl ketimines can be readily prepared from the direct condensation of *N*-*tert*-butanesulfinamide with a variety of ketones under mildly Lewis acidic conditions.[6] Our first objective was to determine whether such conditions would be amenable to the synthesis of **96** from quinone monoketal **95**.

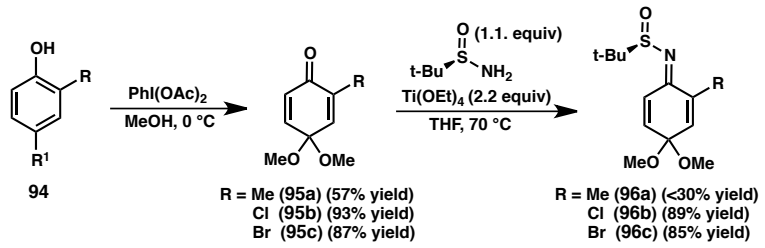


Figure 2. Preparation of quinone-derived sulfinimines.

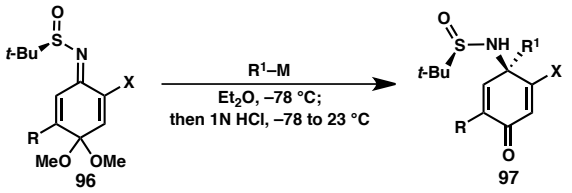
To this end, quinone monoketals **95a-95c** were prepared in one step by oxidation of the corresponding phenols (Figure 2). Our preliminary studies revealed that treatment of **95a** with *N*-*tert*-butanesulfinamide (1.1 equiv) and $Ti(OEt)_4$ (2.2 equiv) in THF at 70 °C for 40 hours furnished sulfinimine **96a**, albeit in low yield. Monitoring the conversion and yield over time indicated that the sulfinimine product was decomposing under the reaction conditions. It was reasoned that utilization of a benzoquinone monoketal bearing an electron-withdrawing substituent would inductively activate the carbonyl towards nucleophilic addition, thereby accelerating the condensation reaction and reducing the

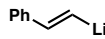
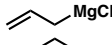
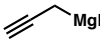
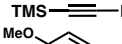
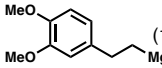
reaction time. Indeed, exposure of **95b** and **95c** to the standard reaction conditions provided **96b** and **96c** in 89% and 85% yield, respectively. In addition to the improved yields of sulfinimine products, halogenated compounds **96b** and **96c** were equipped with functional handles that could be elaborated towards more complex alkaloid intermediates.

With halo-quinone sulfinimines **96b** and **96c** in hand, we turned to evaluating the diastereoselectivity of 1,2-addition reactions of readily available organolithium reagents. To our delight, treatment of chloride **96b** with *n*-BuLi (1.1 equiv) in Et_2O at –78 °C delivered sulfinamide **97a** in 90% yield and 97:3 d.r. (Table 1, entry 1). Importantly, the acidic workup conditions facilitated cleavage of the dimethyl ketal without promoting the formation of dienone migration products. Moreover, the diastereomeric sulfinamide products were easily separated by silica gel chromatography, allowing for the preparation of enantiopure 4-aminocyclohexadienones upon cleavage of the sulfinamide.

High levels of diastereoselectivity were also obtained when bromide **96c** was used (entry 3).[9] A solvent screen revealed ethereal solvents were optimal, with Et_2O or THF providing the highest yields and diastereoselectivities. Use of commercially available alkyllithiums furnished the desired sulfinamides in uniformly high diastereoselectivities for both the chloride and bromide substrates (entries 1, 3-7). On the other hand, 1,2-addition of phenyllithium afforded sulfinamides **97b** and **97h** in moderate d.r. (entries 2 and 8). Interestingly, improved selectivities were observed when *o*-, *m*-, or *p*-tolyllithium was employed (entries 9-11). Vinyl- and alkynyllithium reagents also proved viable nucleophiles for this reaction, providing the corresponding sulfinamides in high d.r. (entries 12, 13, 16). In the case of allyl and propargyl nucleophiles, the readily available Grignard reagents were utilized instead of the corresponding organolithium reagents. The

relative stereochemistry of the newly formed stereogenic center was determined for **97d** by single crystal X-ray diffraction (see Supporting Information) and is consistent with reaction through a closed, chair-like transition state. The stereochemistry of the remaining sulfinamide products was assigned in analogy to **97d**.



entry	X	R		R^1–M (equiv)	pdt	d.r.[a]	yield (%)[b]
1	Cl	H	(**96b**)	*n*-BuLi (1.1)	**97a**	97:3	90
2	Cl	H		PhLi (1.1)	**97b**	78:22	76
3	Br	H	(**96c**)	*n*-BuLi (1.1)	**97c**	98:2	88
4	Br	H		EtLi (1.1)	**97d**	98:2	96
5	Br	H		MeLi (1.1)	**97e**	98:2	91
6	Br	Me	(**96d**)	MeLi (1.1)	**97f**	98:2	91
7	Br	Cl	(**96e**)	MeLi (1.1)	**97g**	97:3	91[c]
8	Br	H		PhLi (1.1)	**97h**	80:20	74
9	Br	H		*o*-MeC_6H_4Li (2.0)	**97i**	97:3	86
10	Br	H		*m*-MeC_6H_4Li (2.0)	**97j**	91:9	79
11	Br	H		*p*-MeC_6H_4Li (2.0)	**97k**	91:9	78
12	Br	H		 (2.0)	**97l**	98:2	68[d]
13	Br	H		 (2.0)	**97m**	98:2	71[d]
14	Br	H		 (1.1)	**97n**	87:13	82[d]
15	Br	H		 (1.1)	**97o**	>97:3	91
16	Br	H		 (2.0)	**97p**	>98:2	99[c,d,e]
17	Br	H		 (1.1)	**97q**	96:4	82[d]

[a]Determined by LCMS. [b]Isolated yield of major diastereomer. [c]Isolated as a mixture of diastereomers. [d]Reaction conducted in THF. [e]Reaction conducted at 0 °C.

Table 1. Scope of diastereoselective 1,2-addition to quinone-derived sulfinimines.

The vinyl halide moiety of the enantioenriched sulfinamide products served as a useful functional handle for further elaboration. For example, vinyl bromide **97e** (R^1 =

Me) undergoes a variety of palladium-catalyzed cross-coupling reactions allowing access to arene-, allyl-, and alkyne-substituted products (Figure 3, **98**, **99**, and **101**, respectively). Alternatively, vinyl bromide **97n** can be coupled with vinyl tributylstannane and treated with Hoveyda-Grubbs second generation catalyst[10] to provide bicycle **100** in excellent yield over two steps.

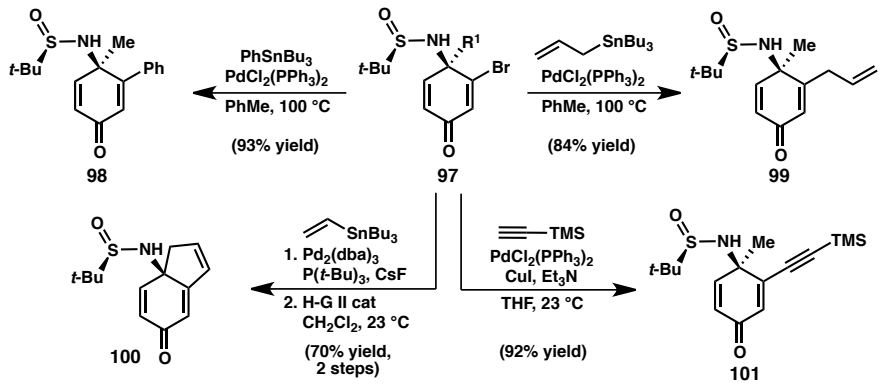


Figure 3. Synthetic transformations of sulfinamide **97**.

Having established a strategy to prepare enantioenriched 4-aminocyclohexadienones, we turned our attention to the synthesis of alkaloid natural products. Although we ultimately sought to target the propellane alkaloids, we recognized that we could readily apply our methodology toward the synthesis of the erythrina alkaloids. Specifically, it was envisioned that the spirocyclic core of 3-(–)-demethoxyerythratidinone (**108**)[11,12] could be derived from **96c** via a one-pot 1,2-addition / intramolecular *N*-alkylation protocol (Figure 4). In the event, addition of aryllithium species **102**[13] to bromosulfinimine **96c** initially generates sulfinamide anion **103**, which upon warming to room temperature delivers spirocycle **104** in 74% yield as a single diastereomer. This

highly convergent reaction provides direct access to the spirocyclic core of **108** with excellent levels of stereocontrol.

To construct the pyrrolidine ring of the natural product, an initial Pd-catalyzed cross-coupling of **104** with vinyl stannane **105** affords enol ether **106** in 85% yield. After considerable experimentation, it was found that brief exposure of **106** to anhydrous HCl in THF at 0 °C resulted in cleavage of the sulfinamide and promoted intramolecular condensation to give indolone **107**. Notably, use of weaker acids or stirring for longer periods resulted in substantially diminished yields due to competitive decomposition of the product. At this point, completion of the synthesis required selective direduction of **107**. In the event, exposure of **107** to heterogeneous hydrogenation conditions furnished **108** in 65% yield. At 6 steps and 26% overall yield, this represents the shortest enantioselective synthesis of **108** reported to date.[14]

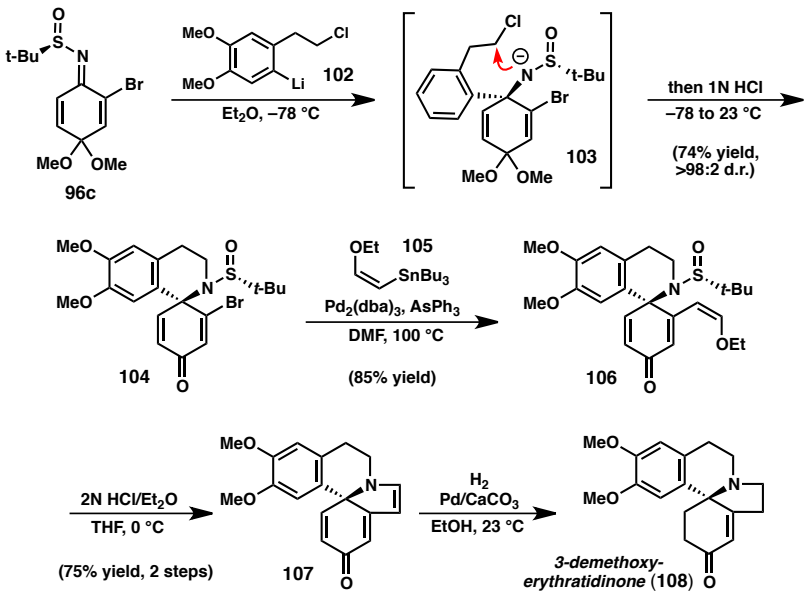


Figure 4. Enantioselective synthesis of (–)-3-demethoxyerythratidinone (**108**).

2.2.3. Synthesis of Hasubanan Alkaloids. Having successfully prepared 3-demethoxyerythratidinone, we turned our attention to the synthesis of the propellane-containing hasubanan alkaloids, initially targeting 8-demethoxyrunanine (**2**)[15] and cepharamine (**1**).[16] Retrosynthetically, an intramolecular Friedel-Crafts-type reaction of dihydroindolone **109** was expected to deliver the propellane core of **2** (Figure 5).[17] On the other hand, we anticipated that intramolecular conjugate addition of **110**, which bears a bromoaryl substituent, should occur from the *o*-position of the arene to deliver the oxidation pattern found in cepharamine. Importantly, the preparation of either dihydroindolone intermediate could be accomplished from sulfinimine **96c** following Grignard addition with an appropriately functionalized nucleophile.

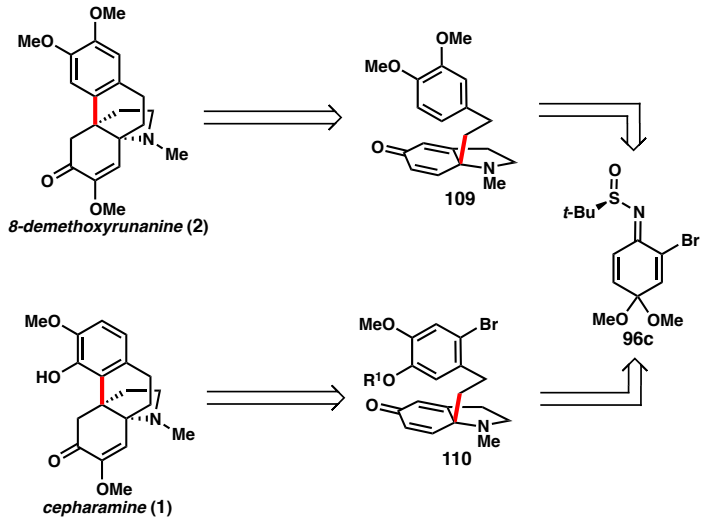


Figure 5. Retrosynthetic analysis for the hasubanan alkaloids.

In the forward sense, addition of Grignard reagent **111** to a solution of sulfinimine **96c** at –78 °C followed by in situ methylation provided sulfinamide **113**, which upon

purification was isolated in 77% as a single diastereomer (Figure 6). In contrast to the previous studies toward 3-demethoxyerythratidinone, AcOH was used for the acidic workup to prevent hydrolysis of the sulfinamide protecting group. Pyrrolidine ring installation was achieved using the previously optimized protocol. Thus, sulfinamide **113** was coupled to vinyl stannane **105** to initially deliver enol ether **115** in excellent yield. Acid-mediated sulfinamide cleavage and cyclization proceeded smoothly to give the corresponding enamine, which was found to be an unstable intermediate. As a result, the crude product was immediately exposed to a mixture of sodium borohydride in AcOH and MeOH to give chromatographically stable dihydroindolone **109** in 96% yield over 2 steps. To access cepharamine, dihydroindolone **117**, which bears a differentially protected phenol, was prepared through an analogous route from **112**.

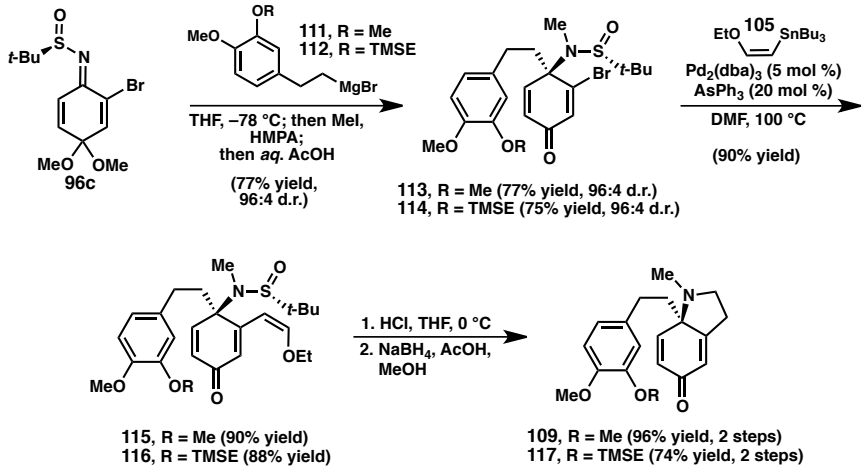


Figure 6. Synthesis of dihydroindolones **109** and **117**.

With dihydroindolones **109** and **117** in hand, we were poised to examine the key intramolecular Friedel-Crafts reaction (Figure 7). After a preliminary screen of Lewis

acids, we were pleased to find that BF_3•OEt_2 promoted the desired cyclization to give propellane **118**, albeit in modest yield. A significant improvement in reactivity was observed when strong Brønsted acids were employed. Indeed, subjection of **109** to triflic acid[18] generates tetracycle **118** as the exclusive cyclization product in 97% yield. The selective addition to the trisubstituted enone olefin is proposed to result from formation of a discrete protonated dienone intermediate that favors the more stable, tertiary carbocation at the C13 position. To access the cepharamine backbone, TMSE-protected phenol **117** was brominated at the C1 position, thereby precluding C1 cyclization to afford the runanine oxidation pattern. Instead, addition of TfOH to the bromide intermediate facilitated cleavage of the TMSE group and cyclization to afford propellane **119**.

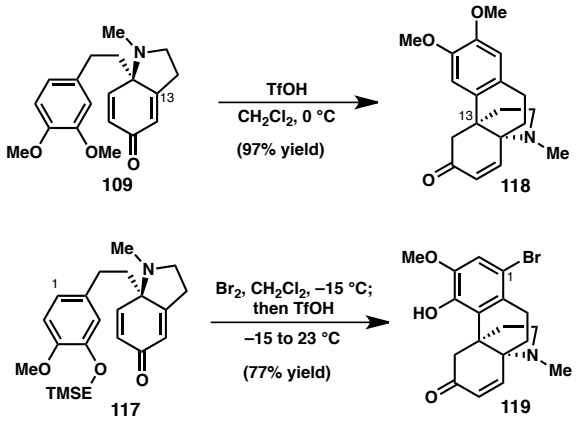


Figure 7. Preparation of aza-propellanes **118** and **119**.

Completion of the syntheses of **1** and **2** required adjustment of the oxidation levels at C7 (Figure 8). Initial attempts to accomplish this objective involved nucelophilic

epoxidation of **118** using hydrogen peroxide and lithium hydroxide in MeOH.[19] Gratifyingly, heating the reaction mixture to 50 °C promoted the formation of 8-demethoxyrunanine (**2**); however, it was isolated in only 15% yield. It was hypothesized that the overall process could be improved by isolating the presumed epoxide intermediate. Under carefully optimized conditions, **118** was cleanly converted to epoxide **120** using *t*-butyl hydroperoxide and Triton B in THF. However, efforts to purify **120** by silica gel chromatography led to isolation of the desired epoxide and an unexpected compound, hemiaminal **121**.[20] Interestingly, prolonged exposure of the crude epoxide to silica gel facilitated conversion to the hemiaminal product, which could now be isolated in 76% yield.

While initially dismayed by this result, we noted that the structural framework of **121** comprises that of the cepharatines, a class of natural products recently reported by Zhang and coworkers.[21] In particular, **121** different from cepharatine D (**123**) by a single oxidation level. With an eye toward completing a synthesis of this new class of natural products, we set out to effect a benzylic oxidation of **121**. Initial attempts to desaturate the C9-C10 bond under radical conditions (e.g., DDQ) failed to provide appreciable amounts of **123**. Given the relative acidity of the C9 protons in **121**, attention was turned to enolization strategies to install the requisite olefin. A survey of reaction conditions revealed that treatment of the potassium enolate of **121** with *N-tert*-butylbenzenesulfinimidoyl chloride (**122**) was optimal,[22] providing cepharatine D in 60% yield.

With access to the cepharatine D, efforts returned to isolation of epoxide **120** en route to 8-demethoxyrunanine. Purification of the crude epoxide on Florisil significantly

suppressed formation of hemiaminal **121**, allowing for isolation of **120** in good yield (Figure 8). From **120**, conversion to the natural product required epoxide opening with MeOH and dehydration to the corresponding enone. After considerable optimization,[23] the epoxide was successfully converted to **2** using tetrabutylammonium methoxide,[24] a reagent found to be uniquely effective for this transformation. Using this route, **2** and cepharatine D (**123**) were both prepared in only 9 steps from commercially available 2-bromo-4-methoxyphenol in 19% and 22% yield, respectively.

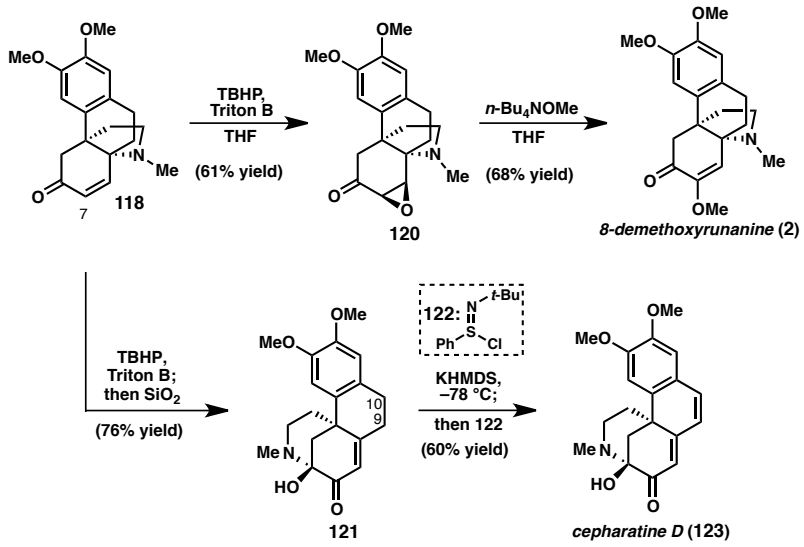


Figure 8. Enantioselective synthesis of 8-demethoxyrunanine and cepharatine D.

After completing a synthesis of **2** and **123**, we turned our attention to the preparation of cepharamine (**1**) from bromo-propellane **119**. Unfortunately, epoxidation of **119** under the previously optimized conditions generated **124** in only 40% yield (Figure 9). Efforts to drive the epoxidation reaction to completion were complicated by competitive oxidative rearrangement of the epoxide product, resulting in the formation of a lactone

byproduct. Moreover, exposure of epoxide **124** to *n*-Bu_4NOMe in THF provided only trace amounts of enol ether **125**. Reasoning that deprotonation of the phenolic O–H might contribute to the poor reactivity observed, several protected variants of **124** were prepared; however, exposure of the corresponding epoxides to a variety of methoxide sources only produced enol ether products in prohibitively low quantities. These studies illustrate how subtle perturbations in the arene oxidation patterns can strikingly alter the reactivity of the aza-propellane framework.

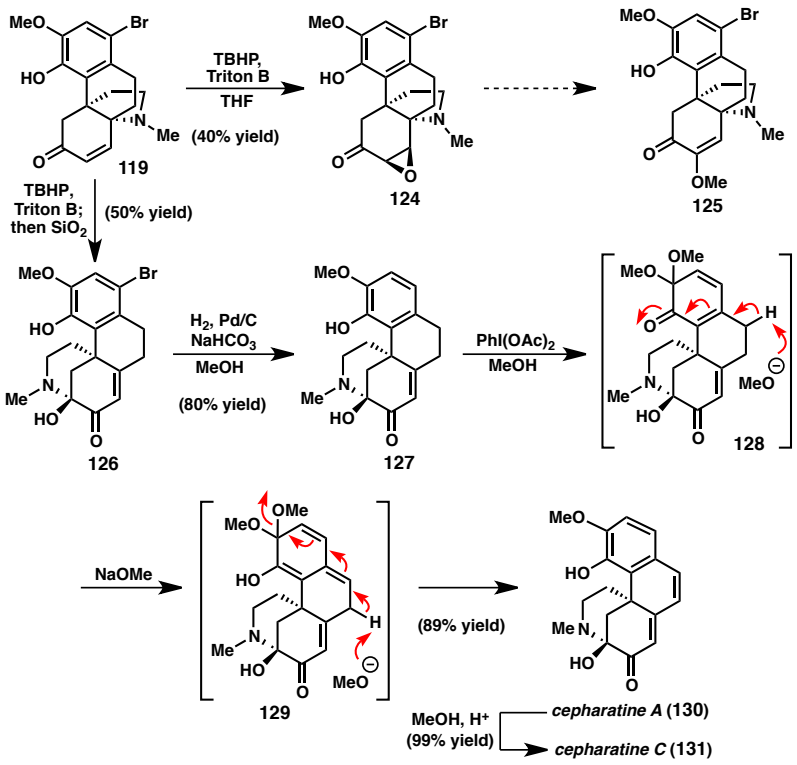


Figure 9. Enantioselective synthesis of cepharatines A and C.

While we were unable to complete a synthesis of cepharamine, we subsequently investigated the conversion of bromo-propellane **119** to cephatines A (**130**) and C (**131**).

Epoxidation of **119** followed by exposure to silica gel provided aminal **126** in 50% yield. Palladium-catalyzed hydrodebromination of **126** proceeded smoothly to generate **127**; however, attempts to oxidize **127** using **122** (see Figure 8) only returned starting material. Rather than protect the phenol moiety, the reactivity of this functional group was exploited to install the desired oxidation. In the event, treatment of phenol **127** with iodobenzene diacetate in MeOH generated *o*-quinone monoketal **128**, which upon rearomatization under basic conditions provided cepharatine A (**130**) in 89% yield. Cepharatine A was readily converted to cepharatine C by exposure to MeOH under acidic reaction conditions. Using this reaction sequence, **130** and **131** could be prepared in 10 and 11 steps, respectively, each in 10% overall yield from commercially available starting materials.

2.3. Concluding Remarks

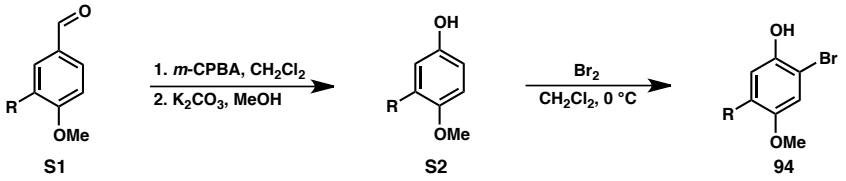
In conclusion, we have developed a unified strategy for the synthesis of 3-demethoxyerythratidinone and several hasubanan alkaloid natural products. Specifically, a highly diastereoselective 1,2-addition of organometallic reagents to benzoquinone-derived *tert*-butanesulfinimines was established, which provides access to enantioenriched 4-aminocyclohexadienone products. This methodology enabled the enantioselective construction of functionalized dihydroindolones, which were found to undergo intramolecular Friedel-Crafts conjugate additions to furnish the propellane cores of several hasubanan alkaloids. As a result of these studies, the first enantioselective total syntheses of 8-demethoxyrunanine and cepharatines A, C, and D were accomplished in 9-11 steps from commercially available starting materials. The versatility of our synthetic

approach is further evidenced in our efforts toward acutumine, a more structurally complex propellane alkaloid. Our synthetic endeavors toward this alkaloid are discussed in the following chapter.

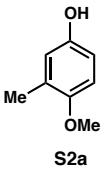
2.4. Experimental Section

2.4.1. Materials and Methods. Unless otherwise stated, reactions were performed under a nitrogen atmosphere using freshly dried solvents. Tetrahydrofuran (THF), methylene chloride (CH_2Cl_2), diethyl ether (Et_2O), acetonitrile (MeCN), and toluene (PhMe) were dried by passing through activated alumina columns. MeOH was distilled over magnesium oxide and triethylamine (Et_3N) was distilled over calcium hydride. All other commercially obtained reagents were used as received unless specifically indicated. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 pre-coated plates (0.25 mm) and were visualized by UV, *p*-anisaldehyde, or $KMnO_4$ staining. Flash column chromatography was performed either as described by Still et al. (Still, W. C., Kahn, M.; Mitra, A. *J. Org. Chem*. **1978**, *43*, 2923-2925) using silica gel (partical size 0.032-0.063) purchased from Silicycle or using pre-packaged RediSep®Rf columns on a CombiFlash Rf system (Teledyne ISCO Inc.). Diastereomeric ratios were determined using an Agilent 1190 or 1290 Series LC/MS (λ = 254 nm) using a ZORBAX Eclipse Plus C18 column (RRHD 1.8 μm, 2.1 x 50 mm, 11,072 plates). Optical rotations were measured on a Jasco P-2000 polarimeter using a 100 mm path-length cell at 589 nm. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury 300 (at 300 MHz and 75 MHz respectively) or a Varian Inova 500 (at 500 MHz and 126 MHz respectively), and are reported relative to internal chloroform (^{1}H, δ = 7.26; ^{13}C, δ = 77.0). Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, app = apparent. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). High-resolution mass spectra were obtained from the Caltech Mass Spectral Facility. HRMS were acquired using an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI), or mixed (MM) ionization mode. Melting points were determined using a Büchi B-545 capillary melting point apparatus and the values reported are uncorrected.

2.4.2. Procedures and Spectroscopic Data.



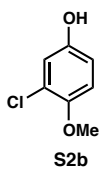
Steps 1 and 2 for phenol preparation: Baeyer-Villiger Oxidation / Saponification. Preparation of 4-methoxy-3-methylphenol (S2a).



S2a

A 50 mL flask was charged with 4-methoxy-3-methylbenzaldehyde (**S1a**) (500 mg, 3.33 mmol, 1 equiv) and CH_2Cl_2 (11 mL). The resulting solution was cooled to 0 °C in an ice-water bath and *m*-CPBA (1.40 g, 70-75%, 5.66 mmol, 1.7 equiv) was added in 3 portions. The resulting suspension was allowed to warm to room temperature, and was stirred for 2 hours at that temperature. The reaction was quenched with saturated aqueous $NaHCO_3$ (11 mL), and the aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated to give a pale yellow oil. The crude formate ester was dissolved in MeOH (17 mL) and cooled to 0 °C. Solid K_2CO_3 (920 mg, 6.66 mmol) was added in one portion, and the resulting solution was stirred at 0 °C for 15 min. The reaction was quenched with aqueous HCl (9 mL of a 2N solution). The organic solvent was removed by rotary evaporation, and resulting aqueous layer was extracted with Et_2O (2 x 30 mL). The combined organic layers were dried over $MgSO_4$, concentrated, and purified by flash chromatography (10% EtOAc/Hexanes) to afford **S2a** (361 mg, 78% yield over 2 steps) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.70 (d, J = 8.8 Hz, 1H), 6.66 (d, J = 3.2 Hz, 1H), 6.62 (dd, J = 8.7, 3.1 Hz, 1H), 4.77 (s, 1H), 3.78 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.0, 149.0, 128.1, 118.0, 112.5, 111.3, 56.0, 16.2; IR (NaCl/thin film): 3350, 2950, 2833, 1501, 1465, 1430, 1286, 1217, 1180, 1034 721 cm^{-1}; HRMS (EI+) calc'd for $C_8H_{10}O_2$ $[M+H]^+$ 138.0681, found 138.0685.

Preparation of 3-chloro-4-methoxyphenol (S2b).

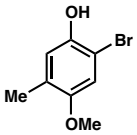


S2b

Prepared from 11.1 mmol of 3-chloro-4-methoxybenzaldehyde (**S1b**) using the above general procedure. The crude product was purified by flash chromatography (5→20% EtOAc/Hexanes) to give **S2b** (1.10 g, 62% yield) as

a beige solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.91 (d, J = 2.9 Hz, 1H), 6.81 (d, J = 8.8 Hz, 1H), 6.70 (dd, J = 8.8, 2.9 Hz, 1H), 4.94 (s, 1H), 3.84 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.6, 149.4, 123.0, 117.6, 114.2, 113.5, 56.8; IR (NaCl/thin film): 3400, 2947, 2837, 1500, 1437, 1278, 1209, 1180, 1058, 907, 746 cm^{-1}; HRMS (EI+) calc'd for $C_7H_7O_2Cl$ $[M+H]^+$ 158.0135, found 158.0125.

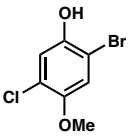
Step 3. Bromination. Preparation of 2-bromo-4-methoxy-5-methylphenol (94d).



94d

A 50 mL flask was charged with phenol **S2a** (300 mg, 2.17 mmol, 1 equiv) and CH_2Cl_2 (11 mL). The resulting solution was cooled to 0 °C in an ice-water bath, and bromine (0.117 mL, 2.28 mmol, 1.05 equiv) was added dropwise. (*Caution! A copious amount of HBr gas is generated as the reaction proceeds. A 16-gauge needle was pierced through the septa to allow the reaction to vent*). The reaction was allowed to stir at 0 °C for 30 min, then quenched with saturated aqueous $NaHCO_3$ (11 mL). The organic layer was washed with water (2 x 10 mL), and the combined aqueous layers were extracted with CH_2Cl_2 (20 mL). The combined organic layers were dried over Na_2SO_4, concentrated, and purified by flash chromatography (10% EtOAc/Hexanes) to give **94d** (440 mg, 93% yield) as a beige solid. The spectral data obtained for **94d** is consistent with that reported in the literature.[25]

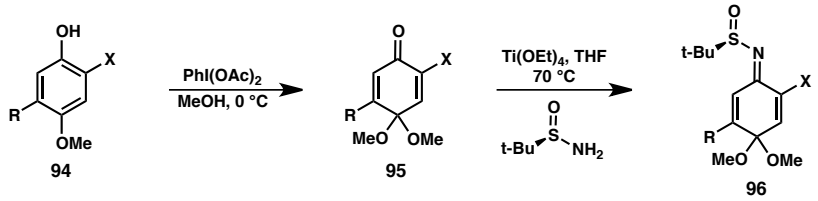
Preparation of 2-bromo-5-chloro-4-methoxyphenol (94e).



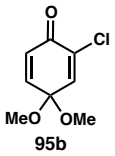
94e

Prepared from 1.26 mmol of phenol **S2b** using the general procedure. **94e** (288 mg, 96% yield) was isolated as a pale beige solid. The crude product was used without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (s, 1H), 7.01 (s, 1H), 5.17 (s, 1H), 3.84 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.5, 146.6, 123.0, 117.6, 115.4, 107.6, 56.9; IR (NaCl/thin film): 3248, 2969, 1504, 1442, 1400, 1205, 1182, 1073, 859, 784 cm^{-1}; HRMS (EI–) calc'd for $C_7H_7O_2Cl$ $[M–H]^-$ 234.9167, found 234.9198.

General procedure for the preparation of quinone sulfinimine substrates:



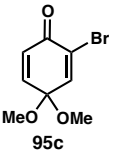
Step 1. Phenolic oxidation. Preparation of chloroquinone 95b.



95b

A 250 mL flask was charged with 2-chloro-4-methoxyphenol (**94b**) (2.00 g, 12.6 mmol, 1.0 equiv) and MeOH (70 mL). The resulting solution was cooled to 0 °C in an ice-water bath and a solution of iodobenzene diacetate (4.47 g, 13.9 mmol, 1.1 equiv) in MeOH (40 mL) was added dropwise via cannula. The reaction was allowed to stir at 0 °C for 10 min, then quenched with saturated aq. $NaHCO_3$ (30mL). The organic solvent was removed by rotary evaporation, and the resulting residue was diluted with Et_2O (60 mL). The aqueous layer was extracted with Et_2O (2 x 50 mL), and the combined organic layers were washed with brine (60 mL), dried over $MgSO_4$, concentrated, and purified by flash chromatography (6:1 Hexanes:EtOAc) to afford **95b** (2.33 g, 98% yield) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.01 (d, J = 2.9 Hz, 1H), 6.85 (dd, J = 10.3, 2.9 Hz, 1H), 6.36 (d, J = 10.3 Hz, 1H), 3.38 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.9, 143.7, 139.3, 134.0, 128.6, 94.2, 50.6; IR (NaCl/thin film): 2943, 2833, 1684, 1647, 1616, 1331, 1118, 1061, 1036, 1018, 962, 948, 824, 812 cm^{-1}; HRMS (EI+) calc'd for $C_8H_9O_3Cl$ $[M+H]^+$ 188.0240, found 188.0211.

Preparation of bromoquinone 95c.

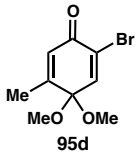


95c

Prepared from 19.7 mmol of 2-bromo-4-methoxyphenol using the general procedure. The quinone product was purified by flash chromatography (10→20% EtOAc/Hexanes) to give **95c** (4.00 g, 87% yield) as a pale yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, J = 3.2 Hz, 1H), 6.82 (dd, J = 10.3 Hz, 3.2 Hz, 1H), 6.33 (d, J = 10.3 Hz, 1H), 3.34 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.6, 143.9, 143.5, 128.0, 125.7, 94.2, 50.5; IR (NaCl/thin film): 3057, 2944, 2834, 1680, 1644, 1612, 1460, 1375, 1332, 1298, 1280, 1221, 1180, 1119, 1062, 1038, 1010, 964,

939, 823, 742 cm^{-1}; HRMS (EI+) calc'd for $C_8H_9O_3Br$ $[M–OMe]^+$ 200.9551, found 200.9551.[26]

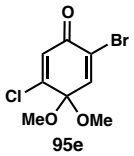
Preparation of bromoquinone 95d.



95d

Prepared from 1.53 mmol of 2-bromo-4-methoxy-5-methylphenol (**94d**) using the general procedure. The quinone product was purified by flash chromatography (0→20% EtOAc/Hexanes) to give **95d** (350 mg, 93% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (s, 1H), 6.33 (q, *J* = 1.5 Hz, 1H), 3.26 (s, 6H), 1.94 (d, *J* = 1.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.7, 156.8, 144.7, 128.0, 127.2, 97.1, 51.2, 16.6; IR (NaCl/thin film): 3315, 3050, 2936, 2832, 1675, 1609, 1437, 1327, 1226, 1104, 1055, 923, 742 cm^{-1}; HRMS (EI+) calc'd for $C_9H_{11}O_3Br$ $[M\text{-}OMe]^+$ 214.9708, found 214.9706.

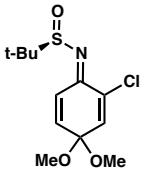
Preparation of dihaloquinone 95e.



95e

Prepared from 0.97 mmol of 2-bromo-5-chloro-4-methoxyphenol (**94e**) using the general procedure. The quinone product was purified by flash chromatography (5→10% EtOAc/Hexanes) to give **95e** (229 mg, 88% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (s, 1H), 6.72 (s, 1H), 3.34 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.1, 153.2, 144.2, 129.5, 126.5, 96.4, 51.7; IR (NaCl/thin film): 3435, 3051, 2940, 2841, 1673, 1612, 1458, 1328, 1105, 1071, 997, 755 cm^{-1}; HRMS (EI+) calc'd for $C_8H_8O_3ClBr$ $[M\text{-}OMe]^+$ 234.9161, found 234.9160.

Step 2. Sulfinamide condensation. Preparation of chlorosulfinimine 96b.

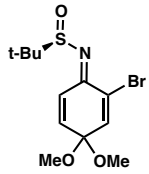


96b

A 50 mL oven-dried Schlenk tube was charged with (*R*)-*tert*-butanesulfinamide (1.78 g, 14.7 mmol, 1.1 equiv) followed by a solution of chloroquinone **95b** (2.64 g, 14.0 mmol, 1.0 equiv) and titanium (IV) ethoxide (6.4 mL, 30.5 mmol, 2.2 equiv) in THF (14 mL). The Schlenk tube was sealed and heated to 70°C in an oil-bath for 72 h while keeping the reaction from light. The reaction was allowed to cool to room temperature, diluted with EtOAc, and slowly poured into a stirring solution of brine (40 mL). The resulting suspension was filtered through a plug of celite and the organic layer was washed with brine (2 x 30 mL). The combined aqueous layers were extracted with EtOAc (40 mL), and the combined

organic layers were dried over Na_2SO_4, concentrated, and purified by flash chromatography (20% EtOAc/Hexanes) to furnish **96b** (3.82 g, 93% yield) as an orange oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 10.7 Hz, 1H), 6.68 (d, *J* = 2.4 Hz, 1H), 6.45 (dd, *J* = 10.5, 2.7 Hz, 1H), 3.34 (s, 3H), 3.33 (s, 3H), 1.33 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.2, 137.0, 134.0, 133.8, 122.3, 94.2, 60.9, 50.3, 50.2, 23.2; IR (NaCl/thin film): 2961, 2945, 1569, 1457, 1168, 1113, 1082, 1039, 957, 790 cm^{-1}; HRMS (EI+) calc'd for $C_{12}H_{18}NO_3ClS$ $[M+H]^+$ 292.0769, found 292.0769; $[\alpha]_D^{25}$ –344.7 (*c* 0.62, CH_2Cl_2).

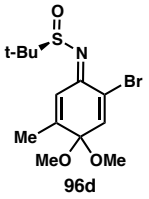
Preparation of bromsulfinimine 96c.



96c

Prepared from 6.44 mmol of bromoquinone **95c** using the general procedure. The sulfinimine product was purified by flash chromatography (9→33% EtOAc/Hexanes) to yield **96c** (1.91 g, 85% yield) as an orange solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 10.7 Hz, 1H), 6.94 (d, *J* = 2.4 Hz, 1H), 6.46 (dd, *J* = 10.5, 2.7 Hz, 1H), 3.35 (s, 3H), 3.34 (s, 3H) 1.33 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.5, 138.4, 137.0, 125.6, 122.1, 94.5, 61.0, 50.33, 50.25, 23.2; IR (NaCl/thin film): 3198, 2958, 2929, 1669, 1597, 1290, 1057, 956, 886 cm^{-1}; HRMS (EI+) calc'd for $C_{12}H_{18}NO_3BrS$ $[M+H]^+$ 336.0264, found 336.0258; $[\alpha]_D^{25}$ –235.6 (*c* 0.80, CH_2Cl_2).

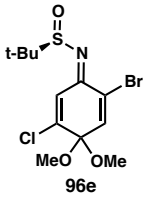
Preparation of quinone sulfinimine 96d.



96d

Prepared from 0.30 mmol of bromoquinone **95d** using the general procedure. The sulfinimine product was purified by flash chromatography (0→20% EtOAc/Hexanes) to yield **96d** (62 mg, 58% yield) as an orange oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (q, *J* = 1.5 Hz, 1H), 6.88 (s, 1H), 3.22 (s, 3H), 3.20 (s, 3H), 1.90 (d, *J* = 1.5 Hz, 3H), 1.34 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.9, 149.5, 139.4, 127.0, 121.6, 97.2, 60.5, 51.1, 51.0, 23.1, 16.8; IR (NaCl/thin film): 2947, 2830, 1611, 1565, 1456, 1362, 1225, 1109, 1079, 969, 939 cm^{-1}; HRMS (EI+) calc'd for $C_{13}H_{20}NO_3SBr$ $[M+H]^+$ 350.0420, found 350.0423; $[\alpha]_D^{25}$ –261.7 (*c* 0.98, CH_2Cl_2).

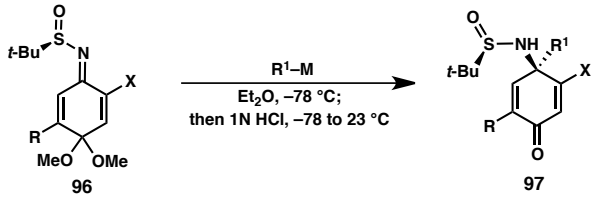
Preparation of quinone sulfinimine 96e.



96e

Prepared from 0.75 mmol of bromoquinone **95e** using the general procedure. The sulfinimine product was purified by flash hromatography (0→20% EtOAc/Hexanes) to yield **96e** (233 mg, 84% yield) as an orange oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (s, 1H), 6.88 (s, 1H), 3.30 (s, 3H), 3.28 (s, 3H), 1.35 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.0, 145.4, 138.5, 126.2, 123.3, 96.4, 61.5, 51.6, 51.5, 23.2; IR (NaCl/thin film): 3078, 2947, 2832, 1596, 1561, 1457, 1363, 1234, 1112, 1081, 1001, 977 cm^{-1}; HRMS (EI+) calc'd for $C_{12}H_{17}NO_3SClBr$ $[M+H]^+$ 369.9874 found 369.9873; $[\alpha]_D^{25}$ –346.2 (*c* 1.54, CH_2Cl_2).

General procedures for the diastereoselective addition of organolithium and organomagnesium reagents to quinone sulfinimine substrates:



96 **97**

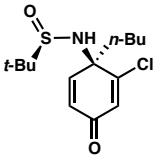
Method A.

An oven-dried 10 mL flask was charged with quinone sulfinimine **96** (0.30 mmol, 1 equiv) and Et_2O (0.6 mL). The resulting solution was cooled to –78 °C in a dry ice-acetone bath, and the organolithium reagent (0.33 mmol, 1.1 equiv) was added dropwise. After stirring at –78 °C for 1 h, the reaction was quenched at that temperature by the addition of aq. 1N HCl (0.6 mL). The reaction mixture was allowed to warm to room temperature and was vigorously stirred for 20 min. The reaction was diluted with EtOAc (30 mL) and washed with saturated aq. $NaHCO_3$ (15 mL). The aqueous layer was extracted with EtOAc (30 mL), and the combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure to provide the crude product, which was analyzed by LC/MS and purified by flash chromatography.

Method B.

An oven-dried 10 mL flask was charged with aryl or vinyl bromide (0.48 mmol, 2.0 equiv) and Et_2O (0.4 mL). The resulting solution was cooled to –78 °C in a dry-ice acetone bath, and *t*-BuLi (0.99 mmol, 1.7 M in pentane, 4.1 equiv) was added dropwise. The resulting solution was warmed to 0 °C and stirred at that temperature for 45 min. The reaction mixture was re-cooled to –78 °C, and a solution of quinone sulfinimine **96** (0.24 mmol, 1 equiv) in Et_2O (0.5 mL) was added dropwise. The resulting suspension was stirred at –78 °C for 1 h, then quenched at that temperature by the addition of aq. 1N HCl (0.5 mL). Reaction work-up was conducted as described in Method A to obtain the crude product, which was analyzed by LC/MS and purified by flash chromatography.

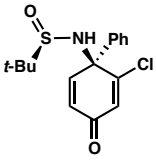
Sulfinamide 97a. Method A.



97a

The reaction was run using quinone sulfinimine **96b** (90 mg, 0.30 mmol) and *n*-BuLi (0.22 mL, 1.5 M in hexanes, 0.33 mmol). The diastereoselectivity was determined by LC/MS: 97:3 d.r. (5→95% $MeCN/H_2O$, t = 0–7 min, 1 mL/min. Minor diastereomer: t_R = 5.3 min, major diastereomer: t_R = 5.6 min). The crude material was purified by flash chromatography (30→80% EtOAc/Hexanes) to provide **97a** (85 mg, 90% yield) as a pale yellow foam. ^1H NMR (500 MHz, $CDCl_3$) δ 6.99 (d, *J* = 10.3 Hz, 1H), 6.53 (d, *J* = 1.5 Hz, 1H), 6.38 (dd, *J* = 10.0, 1.7 Hz, 1H), 3.60 (s, 1H), 2.12 (ddd, *J* = 12.8, 10.5, 6.9 Hz, 1H), 1.67 (ddd, *J* = 12.7, 10.9, 5.5 Hz, 1H), 1.29 (dt, *J* = 14.7, 7.4 Hz, 2H), 1.22 (s, *J* = 5.0 Hz, 9H), 1.12 – 1.01 (m, 2H), 0.86 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.2, 155.9, 150.9, 131.0, 128.7, 62.1, 56.7, 38.8, 25.2, 22.4, 22.3, 13.7; IR (NaCl/thin film): 3198, 2959, 2929, 1660, 1599, 1057, 976, 885 cm^{-1}; HRMS (EI+) calc'd for $C_{14}H_{22}NO_2SCl$ $[M+H]^+$ 304.1133, found 304.1131; $[\alpha]_D^{25}$ –160.7 (*c* 0.50, CH_2Cl_2).

Sulfinamide 97b. Method A.

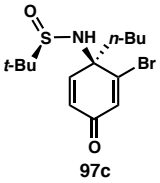


97b

The reaction was run using sulfinimine **96b** (80 mg, 0.27 mmol) and PhLi (0.18 mL, 1.7 M in di-*n*-butyl ether, 0.30 mmol). The diastereoselectivity was determined by LC/MS: 78:22 d.r. (5→95% $MeCN/H_2O$, t = 0–7 min, 1 mL/min. Minor diastereomer: t_R = 4.9 min,

major diastereomer: t_R = 5.1 min). The crude material was purified by flash chromatography (20→80% EtOAc/Hexanes) to give (*R,R*)-**97b** (68 mg, 76% yield) as a pale yellow solid. Major diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49–7.37 (m, 5H), 7.12 (d, *J* = 9.8 Hz, 1H), 6.57 (d, *J* = 1.5 Hz, 1H), 6.40 (dd, *J* = 10.0, 1.7 Hz, 1H), 4.15 (s, 1H), 1.33 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.1, 155.9, 150.5, 137.2, 129.8, 129.4, 129.3, 126.34, 126.23, 64.5, 57.4, 22.6; IR (NaCl/thin film): 3186, 2960, 1658, 1596, 1300, 1062, 976 cm^{-1}; HRMS (EI+) calc'd for $C_{14}H_{22}NO_2ClS$ $[M+H]^+$ 324.0820, found 324.0827; $[\alpha]_D^{25}$ –102.4 (*c* 0.80, CH_2Cl_2). The minor diastereomer ((*R,S*)-**97b**) was obtained as a pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48–7.32 (m, 5H), 6.80 (d, *J* = 10.3 Hz, 1H), 6.74 (d, *J* = 2.0 Hz, 1H), 6.27 (dd, *J* = 10.0, 1.7 Hz, 1H), 4.53 (s, 1H), 1.36 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.1, 158.0, 148.4, 137.5, 129.8, 129.5, 129.2, 126.9, 125.6, 64.3, 57.4, 22.7; IR (NaCl/thin film): 3186, 2960, 1658, 1596, 1491, 1448, 1378, 1364, 1300, 1062, 976, 958 cm^{-1}; HRMS (EI+) calc'd for $C_{14}H_{22}NO_2ClS$ $[M+H]^+$ 324.0820, found 324.0823; $[\alpha]_D^{25}$ –365.9 (*c* 0.40, CH_2Cl_2).

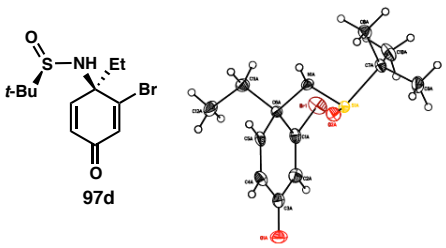
Sulfinamide 97c. Method A.



97c

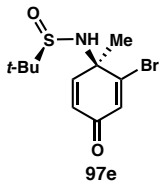
The reaction was run using sulfinimine **96c** (80 mg, 0.24 mmol) and *n*-BuLi (0.18 mL, 1.5 M in hexanes, 0.26 mmol). The diastereoselectivity was determined by LC/MS: 98:2 d.r. (5→95% MeCN/H_2O, t = 0–7 min, 1 mL/min. Minor diastereomer: t_R = 5.4 min, major diastereomer: t_R = 5.7 min). The crude material was purified by flash chromatography (30→90% EtOAc/Hexanes) to furnish **97c** (73 mg, 88% yield) as a pale yellow foam. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (d, *J* = 9.8 Hz, 1H), 6.79 (d, *J* = 2.0 Hz, 1H), 6.41 (dd, *J* = 10.0, 1.7 Hz, 1H), 3.61 (s, 1H), 2.17–2.07 (m, 1H), 1.70–1.59 (m, 2H), 1.35–1.26 (m, 2H), 1.24 (s, 9H), 1.10–1.00 (m, 2H), 0.87 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.5, 151.1, 150.1, 135.3, 128.6, 62.4, 56.8, 39.8, 25.1, 22.6, 22.3, 13.7; IR (NaCl/thin film): 2946, 1567, 1457, 1179, 1110, 1082, 1039, 962, 764 cm^{-1}; HRMS (EI+) calc'd for $C_{14}H_{22}NO_2SBr$ $[M+H]^+$ 348.0627, found 348.0628; $[\alpha]_D^{25}$ –139.0 (*c* 0.50, CH_2Cl_2).

Sulfinamide 97d. Method A.



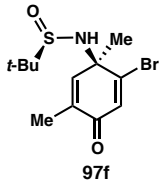
The reaction was run using sulfinimine **96c** (80 mg, 0.24 mmol) and EtLi (0.52 mL, 0.5 M in 90:10 cyclohexane:benzene, 0.26 mmol). The diastereoselectivity was determined by LC/MS: 98:2 d.r. (5→95% MeCN/H_2O, t = 0–7 min, 1 mL/min. Minor diastereomer: t_R = 4.4 min, major diastereomer: t_R = 4.7 min). The crude material was purified by flash chromatography (50→75% EtOAc/Hexanes) to give **97d** (74 mg, 96% yield) as a pale yellow solid. The solid was recrystallized from CH_2Cl_2/pentane to give crystals suitable for single crystal X-ray diffraction. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.07 (d, *J* = 10.3 Hz, 1H), 6.81 (d, *J* = 1.5 Hz, 1H), 6.43 (dd, *J* = 10.0, 1.7 Hz, 1H), 2.14 (dq, *J* = 13.1, 7.5 Hz, 1H), 1.72 (dq, *J* = 13.1, 7.4 Hz, 1H), 1.24 (s, 9H), 0.76 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.5, 150.8, 149.7, 135.6, 128.9, 63.0, 56.8, 33.3, 22.6, 7.5; melting point: 60 °C (decomposition); IR (NaCl/thin film): 3196, 2970, 1669, 1597, 1286, 1052, 954 cm^{-1}; HRMS (EI+) calc'd for $C_{12}H_{18}NO_2SBr$ $[M+H]^+$ 320.0314, found 320.0318. $[\alpha]_D^{25}$ –160.7 (*c* 1.20, CH_2Cl_2).

Sulfinamide 97e. Method A.



The reaction was run using sulfinimine **96c** (90 mg, 0.27 mmol) and MeLi (0.10 mL, 2.9 M in diethoxymethane, 0.29 mmol). The diastereoselectivity was determined by LC/MS: 98:2 d.r. (5→95% MeCN/H_2O, t = 0–7 min, 1 mL/min. Minor diastereomer: t_R = 4.0 min, major diastereomer: t_R = 4.3 min). The crude material was purified by flash chromatography (50→100% EtOAc/Hexanes) to provide **97e** (75 mg, 91% yield) as a pale yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (d, *J* = 10.3 Hz, 1H), 6.74 (d, *J* = 1.5 Hz, 1H), 6.33 (dd, *J* = 10.0, 1.7 Hz, 1H), 3.63 (s, 1H), 1.61 (s, 3H), 1.25 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.1, 151.9, 151.1, 133.9, 126.7, 58.7, 56.8, 28.1, 22.6; IR (NaCl/thin film): 3139, 2991, 1668, 1636, 1599, 1296, 1048, 960, 884 cm^{-1}; HRMS (EI+) calc'd for $C_{11}H_{16}NO_2SBr$ $[M+H]^+$ 306.0158, found 306.0158; $[\alpha]_D^{25}$ –190.3 (*c* 0.71, CH_2Cl_2).

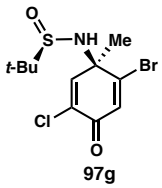
Sulfinamide 97f. Method A.



97f

The reaction was run using sulfinimine **96d** (73 mg, 0.21 mmol) and MeLi (0.08 mL, 2.72 M in diethoxymethane, 0.23 mmol). The diastereoselectivity was determined by LC/MS: 98:2 d.r. (5→95% MeCN/H_2O, t = 0–10 min, 1 mL/min. Minor diastereomer: t_R = 3.0 min, major diastereomer: t_R = 3.3 min). The crude material was purified by flash chromatography (30→80% EtOAc/Hexanes) to provide **97f** (61 mg, 91% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.94 (q, *J* = 1.4 Hz, 1H), 6.72 (s, 1H), 3.59 (s, 1H), 1.93 (d, *J* = 1.5 Hz, 3H), 1.57 (s, 3H), 1.23 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.9, 150.7, 147.4, 133.5, 133.5, 59.0, 56.7, 28.4, 22.6, 15.2; IR (NaCl/thin film): 3125, 2989, 2926, 2870, 1663 1649, 1608, 1460, 1365, 1113, 1040, 1015, 901, 892 cm^{-1}; HRMS (EI+) calc'd for $C_{12}H_{18}NO_2SBr$ $[M+H]^+$ 320.0314, found 320.0316. $[\alpha]_D^{25}$ –168.9 (*c* 1.05, CH_2Cl_2).

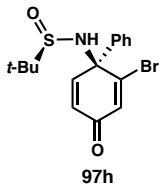
Sulfinamide 97g. Method A.



97g

The reaction was run using sulfinimine **96e** (83 mg, 0.22 mmol) and MeLi (0.091 mL, 2.72 M in diethoxymethane, 0.25 mmol). The diastereoselectivity was determined by LC/MS: 97:3 d.r. (5→95% MeCN/H_2O, t = 0–10 min, 1 mL/min. Minor diastereomer: t_R = 3.1 min, major diastereomer: t_R = 3.4 min). The crude material was purified by flash chromatography (25→70% EtOAc/Hexanes) to provide **97g** (70 mg, 92% yield) as a pale yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (s, 1H), 6.84 (s, 1H), 3.71 (s, 1H), 1.65 (s, 3H), 1.25 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.4, 151.2, 147.8, 132.6, 131.0, 60.6, 57.0, 28.2, 22.5; IR (NaCl/thin film): 3126, 2981, 2930, 2868, 1674, 1609, 1365, 1334, 1040, 1005, 892, 873 cm^{-1}; HRMS (EI+) calc'd for $C_{11}H_{15}NO_2SClBr$ $[M+H]^+$ 339.9768, found 339.9765. $[\alpha]_D^{25}$ –138.1 (*c* 1.2, CH_2Cl_2).

Sulfinamide 97h. Method A.

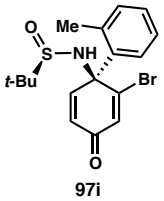


97h

The reaction was run using sulfinimine **96c** (80 mg, 0.24 mmol) and PhLi (0.15 mL, 1.7 M in di-*n*-butyl ether, 0.26 mmol). The diastereoselectivity was determined by LC/MS: 80:20 d.r. (5→95%

MeCN/H_2O, t = 0–7 min, 1 min/mL. Minor diastereomer: t_R = 5.0 min, major diastereomer: t_R = 5.2 min). The crude material was purified by flash chromatography (20→80% EtOAc/Hexanes) to yield (*R,R*)-**97h** (65 mg, 74% yield) as a yellow solid. Major diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 – 7.35 (m, 5H), 7.20 (d, *J* = 9.8 Hz, 1H), 6.83 (d, *J* = 1.5 Hz, 1H), 6.40 (dd, *J* = 10.0, 1.7 Hz, 1H), 4.20 (s, 1H), 1.34 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.4, 150.8, 149.9, 137.6, 133.8, 129.31, 129.25, 126.2, 126.0, 64.8, 57.4, 22.8; IR (NaCl/thin film): 3184, 2960, 1669, 1292, 1059, 954 cm^{-1}; HRMS (EI+) calc'd for $C_{16}H_{18}NO_2SBr$ $[M+H]^+$ 368.0314, found 368.0317. $[\alpha]_D^{25}$ – 102.8 (*c* 0.60, CH_2Cl_2). The minor diastereomer ((*R,S*)-**97h**) was obtained as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 – 7.33 (m, 5H), 6.97 (d, *J* = 2.0 Hz, 1H), 6.89 (d, *J* = 9.8 Hz, 1H), 6.29 (dd, *J* = 10.0, 1.7 Hz, 1H), 4.56 (s, 1H), 1.37 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.3, 152.5, 148.6, 137.9, 133.6, 129.4, 129.2, 126.8, 125.6, 64.8, 57.4, 22.7; IR (NaCl/thin film): 3287, 2959, 1669, 1295, 1078, 952 cm^{-1}; HRMS (EI+) calc'd for $C_{16}H_{18}NO_2SBr$ $[M+H]^+$ 368.0314, found 368.0313; $[\alpha]_D^{25}$ –281.0 (*c* 0.45, CH_2Cl_2).

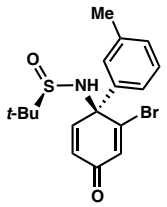
Sulfinamide 97i. Method B.



97i

The reaction was run using quinone sulfinimine **96c** (81 mg, 0.24 mmol), and *o*-bromotoluene (57 μL, 0.48 mmol). The diastereoselectivity was determined by LC/MS: 97:3 d.r. (5% MeCN/H_2O, t = 0–0.5 min; 5→45% MeCN/H_2O, t = 0.5–10.5 min, 1 mL/min. Minor diastereomer: t_R = 8.3 min, major diastereomer: t_R = 8.7 min). The crude material was purified by flash chromatography (25→50% EtOAc/Hexanes) to furnish **97i** (79 mg, 86% yield) as a pale yellow foam. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.34 (dt, *J* = 7.8, 1.5 Hz, 1H), 7.31 (dt, *J* = 7.3, 1.5 Hz, 1H), 7.16 (dd, *J* = 7.3, 1.5 Hz, 1H), 7.10 (d, *J* = 10.3 Hz, 1H), 6.90 (d, *J* = 1.7 Hz, 1H), 6.48 (dd, *J* = 9.9, 1.7 Hz, 1H), 4.23 (s, 1H), 2.26 (s, 3H), 1.32 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.4, 149.3, 148.5, 136.0, 135.7, 134.2, 133.2, 129.3, 127.4, 127.2, 126.9, 64.8, 57.3, 22.7, 20.7; IR (NaCl/thin film): 3188, 2960, 1666, 1641, 1594, 1291, 1082, 1068, 951 cm^{-1}; HRMS (EI+) calc'd for $C_{17}H_{20}NO_2SBr$ $[M+H]^+$ 382.0471, found 382.0469. $[\alpha]_D^{25}$ –107.7 (*c* 0.60, CH_2Cl_2).

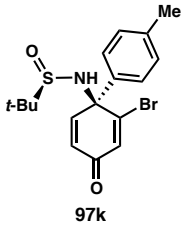
Sulfinamide 97j. Method B.



97j

The reaction was run using sulfinimine **96c** (81 mg, 0.24 mmol) and *m*-bromotoluene (58 μL, 0.48 mmol). The diastereoselectivity was determined by LC/MS: 91:9 d.r. (5→40% MeCN/H_2O, t = 0–0.5 min; 40→50% MeCN/H_2O, t = 0.5–8.5 min, 1 mL/min. Minor diastereomer: t_R = 5.2 min, major diastereomer: t_R = 5.5 min). The crude material was purified by flash chromatography (25→50% EtOAc/Hexanes) to yield **97j** (73 mg, 79% yield) as a pale yellow foam. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.29 (m, 1H), 7.29–7.26 (m, 1H), 7.19 (d, *J* = 10.3 Hz, 1H), 7.19 (m, 1H), 6.83 (d, *J* = 2.0 Hz, 1H), 6.39 (dd, *J* = 9.8, 1.5 Hz, 1H), 4.19 (s, 1H), 2.37 (s, 3H), 1.34 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.5, 150.9, 150.1, 139.3, 137.5, 133.8, 130.1, 129.2, 126.7, 125.9, 123.2, 64.8, 57.4, 22.8, 21.6; IR (NaCl/thin film): 3188, 2959, 1669, 1595, 1292, 1079, 1062, 954 cm^{-1}; HRMS (EI+) calc'd for $C_{17}H_{20}NO_2SBr$ $[M+H]^+$ 382.0471, found 382.0468. $[\alpha]_D^{25}$ –99.1 (*c* 0.60, CH_2Cl_2).

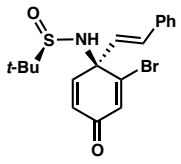
Sulfinamide 97k. Method B.



97k

The reaction was run using sulfinimide **96c** (80 mg, 0.24 mmol) and *p*-bromotoluene (81 mg, 0.48 mmol). The diastereoselectivity was determined by LC/MS: 91:9 d.r. (5→30% MeCN/H_2O, t = 0–0.5 min; 30→50% MeCN/H_2O, t = 0.5–10.5 min, 1 mL/min. Minor diastereomer: t_R = 8.2 min, major diastereomer: t_R = 8.7 min). The crude material was purified by flash chromatography (25→60% EtOAc/Hexanes) to provide **97k** (72 mg, 78% yield) as a pale yellow foam. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (app d, *J* = 8.3 Hz, 2H), 7.22 (d, *J* = 8.3 Hz, 2H), 7.19 (d, *J* = 9.8 Hz, 1H), 6.81 (d, *J* = 1.5 Hz, 1H), 6.38 (dd, *J* = 10.0, 1.7 Hz, 1H), 4.17 (s, 1H), 2.36 (s, 3H), 1.34 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.5, 160.0, 150.2, 139.4, 134.6, 133.7, 130.0, 126.1, 125.8, 64.7, 57.4, 22.8, 21.1; IR (NaCl/thin film): 3186, 2959, 2920, 1668, 1292, 1079, 1062, 955 cm^{-1}; HRMS (EI+) calc'd for $C_{17}H_{20}NO_2SBr$ $[M+H]^+$ 382.0471, found 382.0470. $[\alpha]_D^{25}$ –84.7 (*c* 0.50, CH_2Cl_2).

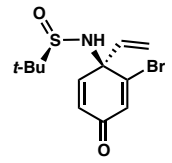
Sulfinamide 97l. Method B.



97l

The reaction was run in THF using sulfinimide **96c** (80 mg, 0.24 mmol) using β-bromostyrene[27] (87 mg, 0.48 mmol). The diastereoselectivity was determined by LC/MS: 98:2 d.r. (5→50% MeCN/H_2O, t = 0–10 min; 50→100% MeCN/H_2O, t = 10–13 min, 1 mL/min. Minor diastereomer: t_R = 11.6 min, major diastereomer: t_R = 11.8 min). The crude material was purified by flash chromatography (25→90% EtOAc/Hexanes) to furnish **97l** (64 mg, 68% yield) as a pale yellow solid.[28] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42–7.37 (m, 2H), 7.37–7.29 (m, 3H), 7.25 (d, *J* = 9.8 Hz, 1H), 6.79 (d, *J* = 1.5 Hz, 1H), 6.69 (d, *J* = 16.1 Hz, 1H), 6.44 (dd, *J* = 10.0, 1.7 Hz, 1H), 6.19 (d, *J* = 16.1 Hz, 1H), 3.92 (s, 1H), 1.30 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.1, 149.7, 149.0, 135.0, 134.0, 133.8, 129.1, 128.8, 127.02, 127.00, 126.9, 62.4, 57.2, 22.7, 22.4; IR (NaCl/thin film): 3189, 2960, 1669, 1596, 1293, 1060, 955, 735 cm^{-1}; HRMS (EI+) calc'd for $C_{18}H_{20}NO_2SBr$ $[M+H]^+$ 394.0471, found 394.0476. $[\alpha]_D^{25}$ –115.0 (*c* 0.65, CH_2Cl_2).

Sulfinamide 97m. Method A.

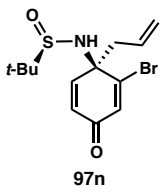


97m

The reaction was run in THF using sulfinimine **96c** (80 mg, 0.24 mmol) and vinyllithium[29] (0.48 mmol). The diastereoselectivity was determined by LC/MS: 98:2 d.r. (5→50% MeCN/H_2O, t = 0–10 min, 1 mL/min. Minor diastereomer: t_R = 7.9 min, major diastereomer: t_R = 8.3 min). The crude material was purified by flash chromatography (40→90% EtOAc/Hexanes) to yield **97m** (55 mg, 72% yield) as a yellow foam. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (d, *J* = 9.8 Hz, 1H), 6.76 (d, *J* = 1.0 Hz, 1H), 6.39 (dd, *J* = 10.0, 1.2 Hz, 1H), 5.87 (dd, *J* = 17.3, 10.5 Hz, 1H), 5.45 (d, *J* = 10.7 Hz, 1H), 5.45 (d, *J* = 17.1 Hz, 1H), 3.82 (s, 1H), 1.27 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.0, 149.6, 148.5, 136.4, 134.1, 127.1, 119.3, 62.6, 57.2, 22.6; IR (NaCl/thin film): 3186, 2959, 1669, 1594, 1294, 1060, 954 cm^{-1}; HRMS (EI+) calc'd for $C_{12}H_{16}NO_2SBr$ $[M+H]^+$ 318.0158, found 318.0161. $[\alpha]_D^{25}$ –175.9 (*c* 0.85, CH_2Cl_2).

Sulfinamide 97n. Method A.

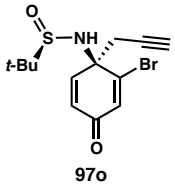
The reaction was run in THF using sulfinimide **96c** (80 mg, 0.24 mmol) and allylmagnesium chloride (0.13 mL, 2.0 M in THF, 0.26 mmol). The diastereoselectivity



97n

was determined by LC/MS: 87:13 d.r. (5→40% MeCN/H_2O, t = 0–0.5 min; 40→60% MeCN/H_2O, t = 0.5–5.5 min, 1 mL/min. Minor diastereomer: t_R = 3.0 min, major diastereomer: t_R = 3.4 min). The crude material was purified by flash chromatography (30→80% EtOAc/Hexanes) to give (*R,R*)-**97n** (49 mg, 82% yield) as a pale yellow solid. Major diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (d, *J* = 10.0 Hz, 1H), 6.79 (d, *J* = 1.8 Hz, 1H), 6.39 (dd, *J* = 10.0, 1.8 Hz, 1H), 5.52 (dddd, *J* = 17.1, 10.1, 7.7, 7.1 Hz, 1H), 5.26–5.22 (m, 1H), 5.22–5.20 (m, 1H), 3.77 (s, *J* = 10.4 Hz, 1H), 2.75 (ddt, *J* = 13.2, 7.1, 1.0 Hz, 1H), 2.57 (ddt, *J* = 13.2, 7.8, 1.0 Hz, 1H), 1.25 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.2, 150.6, 149.7, 135.4, 128.8, 128.2, 122.1, 61.6, 57.1, 44.6, 22.6. IR (NaCl/thin film): 3196, 2959, 1669, 1597, 1056, 957 cm^{-1}; HRMS (EI+) calc'd for $C_{13}H_{18}NO_2SBr$ $[M+H]^+$ 332.0314, found 332.0316. $[\alpha]_D^{25}$ –129.0 (*c* 0.6, CH_2Cl_2). The minor diastereomer ((*R,S*)-**97n**) was obtained as a pale yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.89 (d, *J* = 10.3 Hz, 1H), 6.76 (d, *J* = 1.5 Hz, 1H), 6.39 (dd, *J* = 10.0, 1.7 Hz, 1H), 5.47 (ddt, *J* = 17.1, 10.3, 7.3 Hz, 1H), 5.20 –5.13 (m, 2H), 3.95 (s, 1H), 2.70 – 2.59 (m, 2H), 1.26 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.1, 152.0, 148.3, 133.8, 129.7, 128.7, 121.2, 61.8, 56.9, 43.9, 22.5; IR (NaCl/thin film): 3195, 2956, 1670, 1595, 1070, 955, 883 cm^{-1}; HRMS (EI+) calc'd for $C_{13}H_{18}NO_2S^{81}Br$ $[M+H]^+$ 333.0221, found 333.0209. $[\alpha]_D^{25}$ –95.7 (*c* 0.80, CH_2Cl_2).

Sulfinamide 97o. Method A.

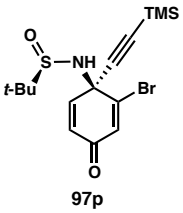


97o

The reaction was run using quinone sulfinimine **96c** (80 mg, 0.24 mmol) and propargylmagnesium bromide (0.48 mL, 0.55 M in Et_2O, 0.26 mmol). The diastereoselectivity was determined to be >97:3 by ^{1}H NMR. The crude material was purified by flash chromatography (25→75% EtOAc/Hexanes) to give **97o** (72 mg, 91% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, *J* = 10.3 Hz, 1H), 6.85 (d, *J* = 1.7 Hz, 1H), 6.40 (dd, *J* = 10.1, 1.8 Hz, 1H), 4.12 (s, 1H), 3.02 (dd, *J* = 16.6, 2.7 Hz, 1H), 2.61 (dd, *J* = 16.6, 2.7 Hz, 1H), 2.27 (t, *J* = 2.7 Hz, 1H), 1.26 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.7, 150.0, 147.7, 136.2, 127.6, 76.0, 74.7, 60.1, 57.2, 31.5, 22.6; IR (NaCl/thin film): 3283,

3128, 2962, 1671, 1600, 1377, 1308, 1278, 1047, 1036, 957 cm^{-1}; HRMS (EI+) calc'd for $C_{13}H_{16}NO_2SBr$ $[M+H]^+$ 330.0158, found 330.0159. $[\alpha]_D^{25}$ –94.6 (*c* 1.05, CH_2Cl_2).

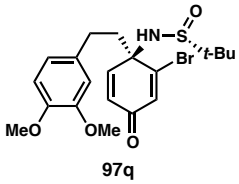
Sulfinamide 97p. Method A.



97p

The reaction was run in THF at 0 °C using quinone sulfinimine **96c** (40 mg, 0.12 mmol) and lithium (trimethylsilyl)acetylide[30] (0.24 mmol). The diastereoselectivity was determined by LC/MS: >98:2 d.r. (30→50% MeCN/H_2O, t = 0–10 min; 50→70% MeCN/H_2O, t = 10–15 min, 1 mL/min. Minor diastereomer: t_R = 11.6 min, major diastereomer: t_R = 12.0 min). The crude material was purified by flash chromatography (10→40% EtOAc/Hexanes) to give **97p** (46 mg, 99% yield) as a pale yellow foam. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (d, *J* = 9.8 Hz, 1H), 6.73 (d, *J* = 1.7 Hz, 1H), 6.36 (dd, *J* = 9.9, 1.7 Hz, 1H), 4.00 (s, 1H), 1.26 (s, 9H), 0.20 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.5, 147.2, 146.1, 133.5, 126.4, 98.1, 93.7, 57.2, 56.5, 22.5, –0.6; IR (NaCl/thin film): 3185, 2960, 1673, 1599, 1292, 1251, 1076, 955, 845 cm^{-1}; HRMS (EI+) calc'd for $C_{15}H_{22}NO_2SSiBr$ $[M+H]^+$ 388.0397, found 388.0401. $[\alpha]_D^{25}$ –41.0 (*c* 0.50, CH_2Cl_2).

Sulfinamide 97q. Method A.

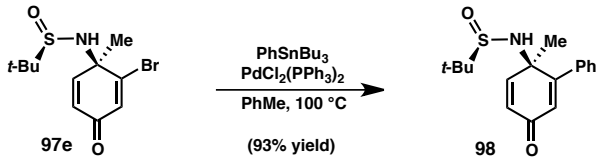


97q

The reaction was run in THF using quinone sulfinimine **96c** (270 mg, 0.80 mmol) and (3,4-dimethoxyphenethyl)magnesium bromide[31] (1.6 mL, 0.55 M in THF, 0.88 mmol). The diastereoselectivity was determined by LC/MS: 96:4 d.r. (30→50% MeCN/H_2O, t = 0–10 min, 1 mL/min. Minor diastereomer: t_R = 5.8 min, major diastereomer: t_R = 7.2 min). The crude material was purified by flash chromatography (50→100% Hexanes/EtOAc) to provide **97q** (301 mg, 82% yield) as a pale yellow foam. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (d, *J* = 10.0 Hz, 1H), 6.87 (d, *J* = 1.7 Hz, 1H), 6.77 (d, *J* = 8.1 Hz, 1H), 6.66 (dd, *J* = 8.1, 2.0 Hz, 1H), 6.62 (d, *J* = 2.0 Hz, 1H), 6.46 (dd, *J* = 10.0, 1.7 Hz, 1H), 3.86 (s, 3H), 3.84 (s, 3H), 3.67 (s, 1H), 2.47 – 2.27 (m, 3H), 2.04 – 1.93 (m, 1H), 1.23 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.3, 150.7, 149.6, 149.0, 147.7, 135.6, 132.0, 128.8, 120.1, 111.5, 111.4, 62.2, 56.8, 56.0, 55.9, 41.8, 29.2, 22.5; IR (NaCl/thin film): 3246, 2958, 2835, 1669, 1645, 1596, 1516, 1465, 1258, 1236, 1157,

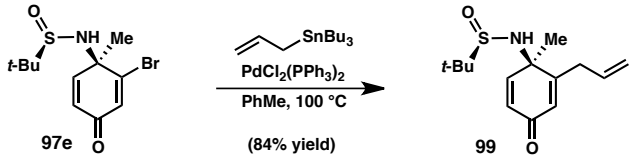
1060, 1027, 730 cm^{-1}; HRMS (EI+) calc'd for $C_{20}H_{26}NO_4SBr$ $[M+H]^+$ 456.0839, found 456.0841. $[\alpha]_D^{25}$ –63.3 (*c* 1.15, CH_2Cl_2).

Preparation of dienone 98.



Sulfinamide **97e** (51.9 mg, 0.169 mmol), $PdCl_2(PPh_3)_2$ (5.6 mg, 8.0 μmol), and $PhSnBu_3$ (75 mg, 0.20 mmol) were dissolved in PhMe (1 mL), and the resulting solution was heated to 100°C for 3 hours. The reaction mixture was cooled to room temperature, filtered through a plug of silica gel, and rinsed with EtOAc (15 mL). The filtrate was concentrated in vacuo and purified by flash chromatography (20→70% CH_2Cl_2/EtOAc) to afford phenyldienone **98** as a white solid (47.8 mg, 0.158 mmol, 93% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 7.50 – 7.47 (m, 2H), 7.37–7.35 (m, 3H), 7.09 (d, *J* = 10.0 Hz, 1H), 6.37 (d, *J* = 2.0 Hz, 1H), 6.30 (dd, *J* = 10.0 Hz, 2.0 Hz, 1H), 3.55 (s, 1H), 1.72 (s, 3H), 1.03 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.7, 159.5, 154.0, 137.2, 129.5, 129.1, 128.6, 128.2, 126.2, 57.4, 56.6, 28.0, 22.3; IR (NaCl/thin film): 3434, 3151, 2986, 2958, 2930, 2868, 1660, 1626, 1570, 1472, 1457, 1364, 1290, 1274, 1147, 1114, 1040, 893, 813, 763, 705 cm^{-1}; HRMS (ES+) calc'd for $C_{17}H_{22}NO_2S$ $[M+H]^+$ 304.1366, found 304.1358; $[\alpha]_D^{25}$ –134.2 (*c* 0.81, CH_2Cl_2).

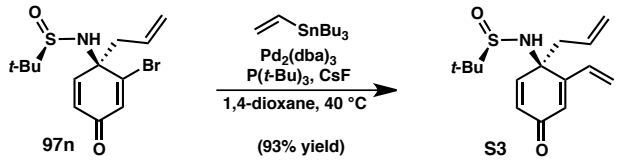
Preparation of dienone 99.



Sulfinamide **97e** (48 mg, 0.16 mmol), $PdCl_2(PPh_3)_2$ (5.5 mg, 7.8 μmol), and allyltributyltin (62 mg, 0.19 mmol) were dissolved in PhMe (1 mL), and the resulting solution was heated to 100°C for 3 hours. The reaction mixture was cooled to room temperature, filtered through a plug of silica gel, and rinsed with EtOAc (15 mL). The

resulting solution was concentrated in vacuo and the crude residue was purified by flash chromatography (20→70% EtOAc/CH_2Cl_2) to afford dienone **99** (35.1 mg, 0.131 mmol, 84% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.96 (d, *J* = 10.0 Hz, 1H), 6.22 (dd, *J* = 9.8, 2.0 Hz, 1H), 6.19 (app. q, *J* = 1.6 Hz, 1H), 5.75 (m, 1H), 5.20 (dq, *J* = 10.0, 1.2 Hz, 1H), 5.14 (dq, *J* = 17.0, 1.5 Hz, 1H), 3.55 (s, 1H), 3.15 (dddd, *J* = 17.3, 6.3, 2.8, 1.4 Hz, 1H), 2.99 (dddd, *J* = 17.3, 7.3, 2.3, 1.3 Hz, 1H), 1.48 (s, 3H), 1.20 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.5, 160.5, 153.6, 133.5, 128.4, 126.7, 118.9, 57.2, 56.4, 34.7, 26.3, 22.5; IR (NaCl/thin film): 3128, 2983, 2964, 2928, 2870, 1672, 1635, 1460, 1419, 1388, 1363, 1285, 1270, 1157, 1064, 1043, 916, 892, 810 cm^{-1}; HRMS (ES+) calc'd for $C_{14}H_{22}NO_2S$ $[M+H]^+$ 268.1366, found 268.1376. $[\alpha]_D^{25}$ –82.7 (*c* 0.70, CH_2Cl_2).

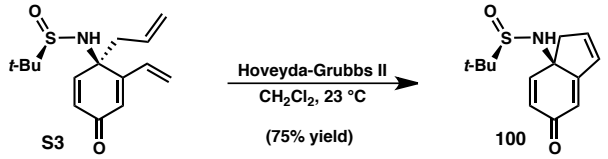
Preparation of trienone S3.



Sulfinamide **97n** (100 mg, 0.30 mmol), $Pd_2(dba)_3$ (4.1 mg, 0.0045 mmol), P(*t*-Bu)$_3$ (3.7 mg, 0.018 mmol), CsF (101 mg, 0.66 mmol), and vinyltributylstannane (93μL, 0.32 mmol), and 1,4-dioxane (3.0 mL) were sequentially added to a Schlenk tube. The solution was then stirred and degassed via 3 freeze-pump-thaw cycles, then heated to 40°C for 20 hours. The solution was cooled and filtered through a plug of silica, rinsed with EtOAc (30 mL), and concentrated to afford a brown oil. Flash chromatography (1→5% MeOH/CH_2Cl_2) afforded trienone **S3** (78 mg, 0.28 mmol, 93% yield) as a bright yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.89 (d, *J* = 10.1 Hz, 1H), 6.46 (d, *J* = 1.8 Hz), 6.42 (ddd, *J* = 17.4, 11.0, 0.6 Hz, 1H), 6.23 (dd, *J* = 10.1, 2.0 Hz, 1H), 5.79 (dd, *J* = 17.5, 1.0 Hz, 1H), 5.40 (dd, *J* = 11.0, 1.0 Hz, 1H), 5.45–5.35 (m, 1H), 5.08–5.00 (m, 2H), 3.88 (s, 1H), 2.55–2.43 (m, 2H), 1.11 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.9, 155.3, 151.8, 132.1, 129.5, 127.9, 125.7, 121.1, 120.8, 59.0, 56.5, 43.5, 22.5; IR (NaCl/thin film): 3197, 2980, 2960, 2234, 1663, 1624, 1474, 1420, 1390, 1364, 1295, 1192, 1175,

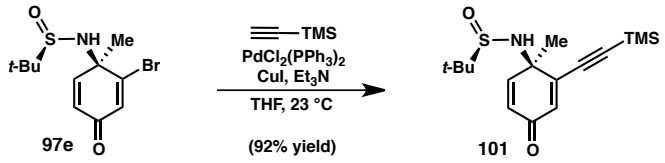
1154, 1057, 992, 9224, 895, 818, 734 cm^{-1}; HRMS (ES+) calc'd for $C_{15}H_{22}NO_2S$ $[M+H]^+$ 280.1366, found 280.1376; $[\alpha]_D^{25}$ –247.5 (*c* 0.92, CH_2Cl_2).

Preparation of bicycle 100.



To a solution of trienone **S3** (18 mg, 0.065 mmol) in CH_2Cl_2 (0.75 mL) was added Hoveyda-Grubbs II catalyst (2.6 mg, 4.6 μmol). The solution was stirred at 23°C for 3 hours, then concentrated and purified by flash chromatography (1→5% MeOH/CH_2Cl_2) to afford bicycle **100** (14 mg, 0.058 mmol, 88% yield) as a white crystalline solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (dd, *J* = 9.8, 0.7 Hz, 1H), 6.58 (dt, *J* = 5.2 Hz, 2.6 Hz, 1H), 6.47 (dt, *J* = 5.8, 2.0 Hz, 1H), 6.25 (dd, *J* = 9.8, 1.7 Hz, 1H), 6.13 (d, *J* = 1.5 Hz, 1H), 3.43 (s, 1H), 2.77 (t, *J* = 2.2 Hz, 2H), 1.12 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.3, 166.7, 145.5, 143.7, 130.9, 130.6, 120.2, 61.7, 56.4, 43.4, 22.3; IR (NaCl/thin film): 3152, 2979, 2918, 2866, 1726, 1653, 1634, 1597, 1561, 1474, 1457, 1379, 1362, 1289, 1190, 1050, 1037, 929, 891, 865, 811, 740 cm^{-1}; HRMS (ES+) calc'd for $C_{13}H_{17}NO_2S$ $[M+H]^+$ 252.1058, found 252.1061; $[\alpha]_D^{25}$ –80.4 (*c* 0.29, CH_2Cl_2).

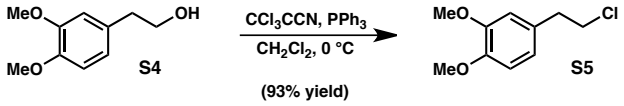
Preparation of dienone 101.



A 10 mL flask was charged with sulfinamide **97e** (50 mg, 0.16 mmol), $PdCl_2(PPh_3)_2$ (6.0 mg, 8 μmol), CuI (3.0 mg, 16 μmol), and THF (0.8 mL). Nitrogen was bubbled through the resulting suspension for 20 minutes, then Et_3N (0.8 mL) and ethynyltrimethylsilane (25 μL, 0.18 mmol) were added. The reaction mixture was allowed to stir 1 hour at room temperature, then filtered through Celite, rinsed with EtOAc, concentrated, and purified by flash chromatography (0→70% EtOAc/CH_2Cl_2) to

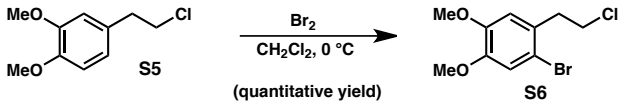
provide dienone **101** (49 mg, 92% yield) as a pale yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.01 (d, *J* = 10.1 Hz, 1H), 6.44 (d, *J* = 2.0 Hz, 1H), 6.28 (dd, *J* = 10.3, 2.0 Hz, 1H), 3.62 (s, 1H), 1.60 (s, 3H), 1.22 (s, 9H), 0.21 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.7, 152.1, 143.7, 133.6, 127.5, 107.4, 100.8, 56.4, 56.3, 27.9, 22.4, –0.5; IR (NaCl/thin film): 3139, 2960, 2253, 2149, 1662, 1623, 1586, 1364, 1251, 1105, 1043, 897, 843 cm^{-1}; HRMS (ES+) calc'd for $C_{16}H_{25}NO_2SSi$ $[M+H]^+$ 324.1454, found 324.1463; $[\alpha]_D^{25}$ –191.8 (*c* 1.13, CH_2Cl_2).

Preparation of 3,4-dimethoxyphenethyl chloride (S5).



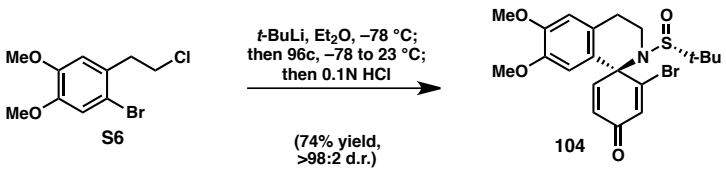
To a solution of 3,4-dimethoxyphenethanol (**S4**) (4.72g, 25.9 mmol) in CH_2Cl_2 (250 mL) at 0°C was added PPh_3 (13.6 g, 51.8 mmol). The solution was stirred for 10 minutes, and CCl_3CCN (3.89 mL, 38.9 mmol) was added dropwise via syringe over 5 minutes. The solution was stirred at 0 °C for 10 min and then slowly warmed to room temperature. After stirring for an additional 45 minutes, the reaction mixture was concentrated and purified by flash chromatography (5→20% EtOAc/Hexanes) to afford chloride **S5** (4.82 g, 24.0 mmol, 93 % yield) as a clear colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.81 (d, *J* = 8.30 Hz, 1H), 6.76 (dd, *J* = 8.1, 2.0 Hz, 1H), 6.73 (d, *J* = 2.0 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.68 (t, *J* = 7.5 Hz, 2H), 3.00 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.9, 147.9, 130.6, 120.7, 112.0, 111.2, 55.8, 55.8, 45.1, 38.7; IR (NaCl/thin film): 3000, 2956, 2909, 2867, 2934, 1607, 1591, 1516, 1464, 1418, 1325, 1260, 1232, 1191, 1146, 1027, 914, 854, 809, 767 cm^{-1}; HRMS (ES+) calc'd for $C_{10}H_{13}O_2Cl$ $[M+H]^+$ 200.0604, found 200.0591.

Preparation of 2-bromo-3,4-dimethoxyphenethyl chloride (S6).



To a solution of chloride **S5** (4.82 g, 24.0 mmol) in CH_2Cl_2 (240 mL) at 0°C was added bromine (1.25 mL, 24.2 mmol) dropwise via syringe. (*Caution! A copious amount of HBr gas is generated as the reaction proceeds. A needle was pierced through the septa to allow the reaction to vent*). The solution was stirred at 0°C for 10 minutes, warmed to room temperature, and stirred for another 20 minutes. The reaction mixture was quenched with saturated aqueous $Na_2S_2O_3$ (50 mL) and washed with saturated $NaHCO_3$ (3 x 100 mL). The combined aqueous layers were extracted with CH_2Cl_2 (50 mL), and the combined organic layers were dried over Na_2SO_4, concentrated, and purified by flash chromatography (5→20% EtOAc/Hexanes) to afford bromide **S6** (6.70 g, 24.0 mmol, quantitative yield) as white needles. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.01 (s, 1H), 6.77 (s, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.71, (t, *J* = 7.3 Hz, 2H), 3.12 (t, *J* = 7.3 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.6, 148.3, 129.2, 115.6, 114.2, 113.9, 56.2, 56.1, 43.5, 39.1; IR (NaCl/thin film): 3009, 2955, 2940, 2906, 2836, 1602, 1576, 1510, 1469, 1461, 1451, 1435, 1382, 1344, 1266, 1254, 1217, 1166, 1033, 959, 856, 834, 865, 834, 802, 759 cm^{-1}; HRMS (ES+) calc'd for $C_{10}H_{12}O_2Cl^{81}Br$ $[M+H]^+$ 279.9689, found 279.9691.

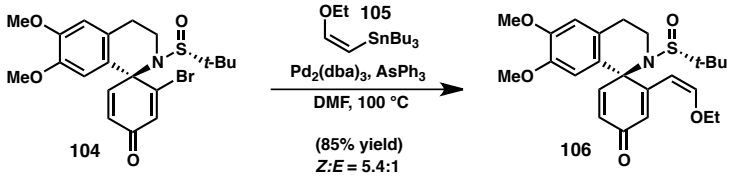
Preparation of sulfinamide 104.



To a solution of aryl bromide **S6** (506 mg, 1.8 mmol) in Et_2O (18 mL) at –78°C was added a solution of *t*-BuLi (1.6 M in pentane, 1.31 mL, 2.1 mmol) dropwise via syringe, and the resulting mixture was stirred 2 hours at –78 °C. A solution of sulfinimine **96c** (495 mg, 1.5 mmol) in Et_2O (3 mL) was added over 5 minutes. The reaction mixture was stirred 1 hour at –78°C, then allowed to warm to room temperature and stirred for an additional hour. The reaction was quenched by the slow addition of aqueous HCl (0.1 N) and stirred for 30 minutes. The biphasic mixture was diluted with EtOAc (60 mL) and washed with saturated aqueous $NaHCO_3$ (3 x 20 mL). The combined aqueous layers were back extracted with EtOAc (1 x 25 mL), and the combined organic layers were dried over Na_2SO_4 and concentrated to give a light brown oil. The diastereoselectivity was

determined by LC/MS: >98:2 d.r. (5→95% MeCN/H_2O, t = 0–10 min, 1 mL/min. Minor diastereomer: t_R = 3.7 min, major diastereomer: t_R = 4.0 min). Flash chromatography (10→30% EtOAc/CH_2Cl_2) afforded tricyclic dienone **104** (491 mg, 1.08 mmol, 74% yield) as an off-white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, *J* = 9.8Hz, 1H), 6.77 (d, *J* = 1.5 Hz, 1H), 6.63 (s, 1H), 6.42 (dd, *J* = 9.8, 1.5 Hz, 1H), 6.32 (s, 1H), 3.86 (s, 3H), 3.72 (s, 3H), 3.52 (dt, *J* = 13.2, 4.4 Hz, 1H), 3.33 (ddd, *J* = 13.2, 9.8, 2.9 Hz, 1H), 3.03 (ddd, *J* =15.4, 10.0, 3.9 Hz, 1H), 2.79 (dt, *J* = 15.4, 3.8 Hz, 1H), 1.30 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.7, 153.0, 149.6, 149.1, 148.3, 133.5, 128.5, 126.0, 122.7, 111.5, 109.1, 66.7, 59.2, 56.1, 55.8, 38.5, 29.0, 24.4; IR (NaCl/thin film): 2958, 2925, 2855, 1669, 1644, 1594, 1516, 1436, 1363, 1298, 1262, 1230, 1199, 1126, 1076, 1022, 954, 915, 796, 731 cm^{-1}; HRMS (EI+) calc'd for $C_{20}H_{24}BrNO_4S$ $[M+H]^+$ 454.0682, found 454.0697; $[\alpha]_D^{25}$ –17.3 (*c* 0.39, CH_2Cl_2).

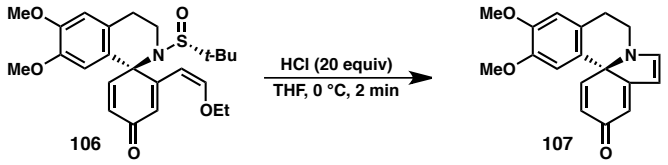
Preparation of trienone 106.



To a solution of dienone **104** (238 mg, 0.52 mmol) in DMF (10 mL) was added $Pd_2(dba)_3$ (14 mg, 0.016 mmol), $AsPh_3$ (19 mg, 0.063 mmol) and stannane **105** (164 mg, 0.63 mmol). N_2 was then bubbled through the solution for 30 minutes, and the reaction was then stirred at 100°C for 1 hour. Upon cooling to room temperature, the reaction mixture was passed through a plug of Celite, rinsed and diluted with Et_2O (40 mL), and washed with H_2O (3 x 50 mL). The combined organic layers were dried over $MgSO_4$, concentrated, and purified by flash chromatography (35→100% EtOAc/Hexanes) to afford trienone **106** (~5.4:1 mixture of *Z:E*-isomers by ^{1}H NMR) as a tan solid (199 mg, 0.446 mmol, 85% yield). *Z*-**106**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (d, *J* = 10.0 Hz, 1H), 7.13 (d, *J* = 2.0 Hz, 1H), 6.59 (s, 1H), 6.36 (dd, *J* = 10.0, 2.0 Hz, 1H), 6.34 (s, 1H), 6.28 (d, *J* = 7.3 Hz, 1H), 4.46 (d, *J* = 7.1 Hz, 1H), 3.97–3.90 (m, 2H), 3.84 (s, 3H), 3.67 (s, 3H), 3.49 (ddd, *J* = 13.1, 4.3, 3.4 Hz, 1H), 3.17 (ddd, *J* = 13.1, 11.3, 2.8 Hz, 1H), 3.05

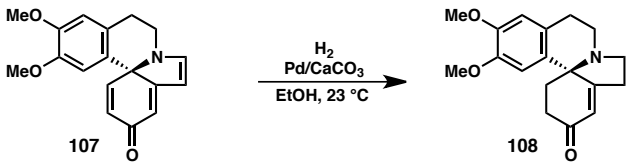
(ddd, *J* = 15.5, 11.2, 4.0 Hz, 1H), 2.81 (dt, *J* = 15.5, 3.0 Hz, 1H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.19 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 187.4, 155.4, 153.3, 148.5, 148.1, 147.3, 127.6, 127.2, 126.8, 125.0, 111.3, 109.9, 102.8, 70.4, 63.9, 58.4, 56.0, 55.8, 38.1, 29.0, 24.1, 15.4. IR (NaCl/thin film): 2979, 2959, 2932, 1658, 1625, 1574, 1516, 1464, 1360, 1262, 1249, 1124, 1072, 1038, 1021, 893, 795 cm^{-1}; HRMS (ES+) calc'd for $C_{24}H_{32}NO_5S$ $[M+H]^+$ 446.1996, found 446.2006. *E*-**106** gave the following diagnostic resonances by ^{1}H NMR (500 MHz, $CDCl_3$): 7.18 (d, *J* = 10.0 Hz, 1H), 6.89 (d, *J* = 13.0 Hz, 1H), 5.09 (d, *J* = 13.2 Hz).

Preparation of enamine 107.



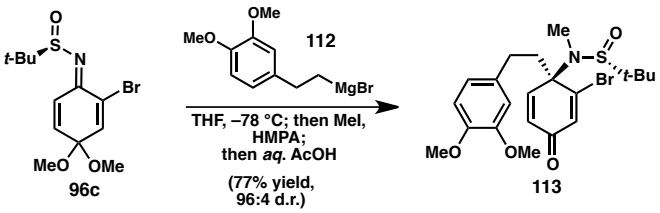
To a solution of trienone **106** (50 mg, 0.11 mmol) in THF (2.2 mL) at 0 °C was added a solution of HCl (2.0 M solution in Et_2O, 1.1 mL, 2.2 mmol) dropwise by syringe. The reaction was allowed to stir 2 min at 0 °C, then quenched by the addition of aq. NaOH (10% w/w, 4 mL) and stirred for an additional 5 minutes. The mixture was diluted with H_2O (5 mL) and extracted with EtOAc (4 x 10 mL). The combined organic layers were dried over Na_2SO_4, concentrated, and purified by flash chromatography (10→20% EtOAc/ CH_2Cl_2) to afford enamine **107** (29 mg, 0.098 mmol, 88% yield) as a bright orange solid. $[\alpha]^{25}_D$ –1307 (*c* 0.72, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.02 (d, *J* = 9.8 Hz, 1H), 6.99 (d, *J* = 3.4 Hz, 1H), 6.85 (s, 1H), 6.53 (s, 1H), 6.06 (dd, *J* = 9.8 Hz, 2.0 Hz, 1H), 6.03 (d, *J* = 1.5 Hz, 1H), 5.62 (d, *J* = 3.4 Hz, 1H), 3.83 (s, 1H), 3.78 (ddd, *J* = 14.2 Hz, 6.8 Hz, 1.0 Hz, 1H), 3.74 (s, 1H), 3.56 (ddd, *J* = 14.2 Hz, 12.7 Hz, 4.4 Hz, 1H), 2.93 (ddd, *J* = 16.9 Hz, 12.5 Hz, 6.4 Hz, 1H), 2.75 (dd, 16.4 Hz, 4.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.5, 172.8, 152.9, 148.6, 148.0, 143.6, 127.8, 125.7, 124.6, 112.7, 111.4, 107.5, 105.2, 71.3, 55.9, 55.8, 42.1, 28.5; IR (NaCl/thin film): 2992, 2955, 2936, 2835, 1636, 1605, 1571, 1523, 1513, 1455, 1450, 1442, 1402, 1356, 1333, 1256, 1218, 1204, 1190, 1166, 1140, 1111, 1081, 1068, 1039, 1001, 895, 852, 784, 731 cm^{-1}; HRMS (ES+) calc'd for $C_{18}H_{18}NO_3$ $[M+H]^+$ 296.1281, found 296.1272.

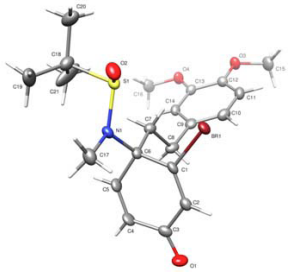
Preparation of (–)-3-demethoxyerythratidinone (108).



To a solution of enamine **107** (20 mg, 0.068 mmol, 1.0 equiv) in EtOH (3.3 mL) was added Pd on $CaCO_3$ (14 mg, 5 wt %, 7.0 μmol, 0.1 equiv). The solution was placed under an atmosphere of H_2 and was stirred 3 hours at room temperature. The reaction was filtered through a plug of Celite, rinsed with EtOAc, concentrated, and purified by flash chromatography (0→20% acetone/CH_2Cl_2) to afford (–)-3-demethoxyerythratidinone (**108**) as a pale yellow oil (13 mg, 0.043 mmol, 65% yield). $[\alpha]^{25}_D$ –296.5 (*c* 0.57, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.65 (s, 1H), 6.56 (s, 1H), 6.11 (app. s, 1H), 3.86 (s, 3H), 3.75 (s, 3H), 3.49 (ddd, *J* = 14.4, 11.7, 6.6 Hz, 1H), 3.24 (dd, *J* = 14.4 Hz, 7.6 Hz, 1H), 3.12–3.00 (m, 2H), 2.86 (q, *J* = 7.7 Hz, 1H), 2.77–2.68 (m, 1H), 2.62–2.50 (m, 3H), 2.46 (dd, *J* = 18.3, 4.2 Hz, 1H), 2.31 (ddd, *J* = 12.5, 5.6, 2.0 Hz, 1H), 2.24 – 2.15 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.5, 169.2, 148.3, 146.8, 125.7, 124.8, 123.4, 112.8, 110.3, 63.5, 56.0, 55.9, 45.7, 40.1, 36.1, 32.8, 28.7, 21.4; IR (NaCl/thin film): 2928, 2848, 1667, 1509, 1464, 1329, 1253, 1229, 1205, 1165, 1106 cm^{-1}; HRMS (ES+) calc'd for $C_{18}H_{21}NO_3$ $[M+H]^+$ 300.1600, found 300.1606.

Preparation of sulfinamide 113.

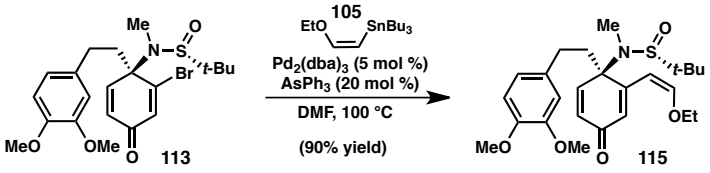




To a solution of sulfinimine **96c** (2.96 g, 8.80 mmol, 1.0 equiv) in THF (17 mL) at –78 °C was added a solution of Grignard reagent **112** (0.67M solution in THF, 14.3 mL, 9.6 mmol) dropwise by syringe. The solution was then stirred at –78 °C for one hour, then MeI (1.6 mL, 26.1 mmol, 3.0 equiv) and hexamethylphosphoramide (HMPA) (4.5 mL, 26.1 mmol, 3.0 equiv) were sequentially added by syringe, and the solution stirred at

–78 °C for ten minutes. The solution was then warmed to 23 °C and stirred for 2 hours, then quenched by the addition of aqueous AcOH (10% v/v, 31 mL). After 3.5 hours, the mixture was diluted with H_2O (100 mL) and extracted with EtOAc (3 x 150 mL) and washed with H_2O (3 x 100 mL). The organic layers were then combined, washed with saturated aqueous $NaHCO_3$ (150 mL), then brine (150 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo to afford a clear brown oil. The diastereoselectivity was determined by LC/MS: 96:4 dr (5→95% MeCN/H_2O, t = 0–10 min, 1 mL/min. Major diastereomer: t_R = 4.2 min, minor diastereomer: t_R = 4.8 min). Flash chromatography (30% to 80% EtOAc in Hexanes) afforded sulfinamide **113** as a white crystalline solid (3.18 g, 6.76 mmol, 77% yield). Recrystallization of **113** by vapor diffusion (CH_2Cl_2 into a solution of **113** in PhMe) afforded crystals suitable for single crystal X-ray diffraction. Melting Point: 136–138 °C; $[\alpha]^{25}_D$: +22.7 (*c* 0.85, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.93 (d, *J* = 1.7 Hz, 1H), 6.82 (d, *J* = 10.0 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.66 (dd, *J* = 6.1 Hz, 2.0 Hz, 2H), 6.62 (d, *J* = 2.0 Hz, 1H), 6.44 (dd, *J* = 9.8 Hz, 1.7 Hz, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 2.81 (td, 12.3 Hz, 4.9 Hz, 1H), 2.47 (s, 3H), 2.39 – 2.24 (m, 2H), 1.84 (td, *J* = 12.5 Hz, 5.2 Hz, 1H), 1.22 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.0, 150.7, 150.1, 148.9, 147.7, 136.4, 132.4, 129.6, 120.1, 111.7, 111.3, 68.7, 59.2, 55.9, 55.8, 38.2, 29.9, 26.7, 24.2; IR (NaCl/thin film): 3042, 2934, 2864, 2833, 1669, 1592, 1516, 1464, 1419, 1377, 1360, 1258, 1238, 1156, 1140, 1077, 1028, 951, 885, 819, 788; HRMS (ES+) calc'd for $C_{21}H_{29}BrNO_4S$ $[M+H]^+$ 470.0995, found 470.1003.

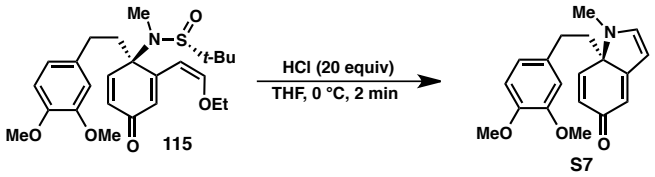
Preparation of enol ether 115.



To a solution of sulfinamide **113** (2.30 g, 4.89 mmol) in DMF (49 mL) was added $Pd_2(dba)_3$ (224 mg, 0.245 mmol, 0.5 equiv), $AsPh_3$ (299 mg, 0.979 mmol, 0.20 equiv), and stannane **105** (1.8 mL, 5.4 mmol, 1.1 equiv). The solution was degassed with N_2 for 30 minutes, then heated and stirred at 100 °C for 1 hour. Upon cooling to room

temperature, the solution was passed through a plug of Celite, diluted with EtOAc (300 mL), and washed with H_2O (3 x 150 mL). The aqueous layers were combined and back-extracted with EtOAc (3 x 100 mL), and the combined organic layers dried over $MgSO_4$, filtered, and concentrated in vacuo to afford brown oil. Flash chromatography (50% to 100% EtOAc in Hexanes) afforded **115** (>10:1 mixture of *Z:E* isomers by ^{1}H NMR) as a tan solid (2.02 g, 4.37 mmol, 91% yield). $[\alpha]_D^{25}$: –80 (*c* 1.07, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (d, *J* = 1.8 Hz, 1H), 6.74 (d, *J* = 8.1 Hz, 1H), 6.54 (d, *J* = 2.0 Hz, 1H), 6.53 (d, *J* = 10.0 Hz, 1H), 6.35 (dd, *J* = 10.0 Hz, 2.0 Hz, 1H), 5.15 (d, *J* = 7.0 Hz, 1H), 4.05 (q, *J* = 7.0 Hz, 2H), 3.81 (s, 3H), 3.81 (s, 3H), 2.53 – 2. 42 (m, 1H), 2.42 (s, 3H), 2.32 – 2.26 (m, 2H), 1.88 – 1.80 (m, 1H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.21 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.6, 154.7, 153.5, 149.4, 148.7, 147.4, 133.3, 130.4, 128.7, 119.9, 111.7, 111.2, 98.7, 70.8, 66.5, 58.8, 55.8, 55.7, 38.3, 29.9, 27.0, 24.4, 15.3; IR (NaCl/thin film): 2958, 2934, 2835, 1660, 1623, 1575, 1516, 1464, 1455, 1303, 1261, 1238, 1180, 1156, 1238, 1180, 1156, 1141, 1099, 1055, 1030, 959, 935, 896, 804, 765, 735; HRMS (EI+) calc'd for $C_{25}H_{36}NO_3S$ $[M+H]^+$ 462.2309, found 462.2320.

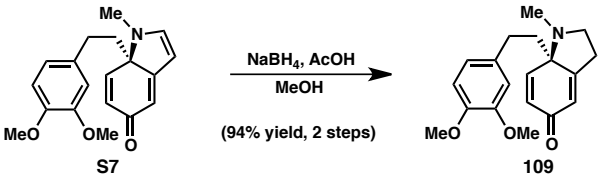
Preparation of enamine S7.



To a solution of enol ether **115** (318.3 mg, 0.668 mmol) in THF (13 mL) at 0 °C was added a solution of hydrochloric acid (2.0 M solution in Et_2O, 7.0 mL, 14 mmol) dropwise by syringe over 1 minute. The reaction was allowed to stir 2 additional minutes at 0 °C and then quenched by the addition of aqueous potassium hydroxide (10% w/v, 10 mL) and stirred an additional 10 minutes. The mixture was diluted with H_2O (10 mL) and extracted with EtOAc (3 x 20 mL). The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a red foam that was used immediately in the next step without further purification. A sample was purified by flash chromatography (1% to 5% MeOH in CH_2Cl_2) for characterization purposes: $[\alpha]_D^{25}$:

–1650 (*c* 0.41, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): 6.98 (dd, *J* = 9.9 Hz, 0.6 Hz, 1H), 6.89 (d, *J* = 3.2 Hz, 1H), 6.73 (d, *J* = 8.3 Hz, 1H), 6.60 (dd, *J* = 8.2 Hz, 2.1 Hz, 1H), 6.56 (d, *J* = 2.2 Hz, 1H), 6.16 (dd, *J* = 9.8 Hz, 1.7 Hz, 1H), 5.88 (d, *J* = 1.5 Hz, 1H), 5.47 (dd, *J* = 3.3, 0.6 Hz, 1H), 3.83 (s, 3H), 3.81 (s, 3H), 3.04 (s, 3H), 2.41–2.30 (m, 2H), 2.08–1.98 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): 184.7, 174.5, 153.4, 148.8, 147.4, 140.1, 132.9, 131.1, 120.1, 111.7, 111.3, 109.8, 99.6, 72.6, 55.8, 55.8, 45.8, 31.5, 29.1. IR (NaCl/thin film): 2934, 2834, 1631, 1592, 1568, 1515, 1465, 1313, 1260, 1237, 1156, 1108, 1089, 1050, 1028, 977, 884, 830, 766; HRMS (ES+) calc'd for $[M+H]^+$ 312.1594, found 312.1585.

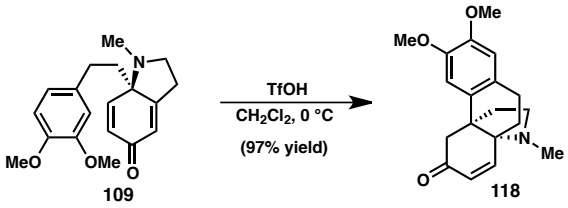
Preparation of dihydroindolone 109.



To a solution of crude enamine **S7** (220 mg) in MeOH (14 mL) at 0 °C was added a solution of $NaBH_4$ (50 mg, 1.32 mmol) in AcOH (5 mL), dropwise by syringe. The solution was stirred at 0 °C for 10 minutes before warming to 20 °C and stirring continued for 1 hour. The reaction was cooled to 0 °C and quenched by the slow addition of potassium hydroxide (30% w/v, 20 mL). The solution was diluted with H_2O (10 mL) and extracted with EtOAc (3 x 20 mL). The organic layers were then combined, dried over Na_2SO_4, filtered, concentrated under reduced pressure to afford an orange oil. Purification by flash chromatography (2% to 4% MeOH in CH_2Cl_2) gave amine **109** as a yellow oil (200 mg, 0.638 mmol, 96% yield over two steps). $[\alpha]_D^{25}$: –40.6 (*c* 0.89, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.96 (d, *J* = 10.0 Hz, 1H), 6.75 (d, *J* = 8.2 Hz, 1H), 6.61 (dd, *J* = 8.2 Hz, 2.1 Hz, 1H), 6.57 (d, *J* = 2.0 Hz, 1H), 6.32 (dd, *J* = 10.0, 1.6 Hz, 1H), 6.18 (dt, *J* = 2.3, 1.5 Hz, 1H), 3.84 (s, 3H), 3.82 (s, 3H), 3.16 (ddd, *J* = 10.5, 8.6, 4.2 Hz, 1H), 3.07–2.99 (m, 1H), 2.81–2.67 (m, 2H), 2.40 (s, 3H), 2.39–2.31 (m, 1H), 2.27–2.17 (m, 1H), 1.90–1.79 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.6, 166.9, 148.8, 147.4, 145.9, 133.6, 130.2, 123.3, 119.8, 111.6, 111.3, 66.5, 55.9, 55.8, 51.6, 36.5,

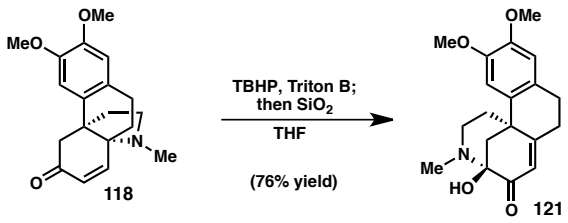
32.0, 29.6, 27.8; IR (NaCl/thin film): 2934, 2834, 2789, 1667, 1642, 1606, 1590, 1515, 1464, 1452, 1418, 1259, 1464, 1452, 1259, 1234, 1176, 1152, 1028, 890, 809, 764; HRMS (EI+) calc'd for $C_{19}H_{24}NO_3$ $[M+H]^+$ 314.1751, found 314.1748.

Preparation of propellane 118.



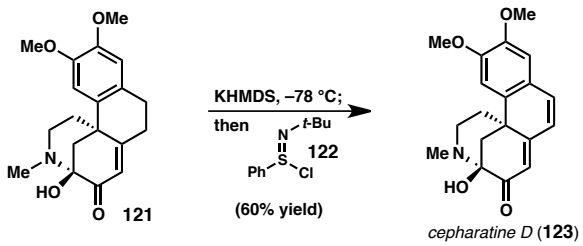
To a solution of dihydroindolone **109** (370 mg, 1.18 mmol, 1.0 equiv) in CH_2Cl_2 (24 mL) at 0 °C was added TfOH (0.522 mL, 5.90 mmol, 5.0 equiv) dropwise by syringe. The solution was stirred for 5 minutes and quenched with saturated aqueous $NaHCO_3$ (50 mL). The mixture was then washed with additional aqueous $NaHCO_3$ (3 x 50 mL), and the combined aqueous layers were back extracted with CH_2Cl_2 (100 mL). The organic layers were then combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford a tan foam. Flash chromatography (1% to 2% MeOH in CH_2Cl_2) afforded propellane **118** as a white foam (360 mg, 1.15 mmol, 97% yield). $[\alpha]_D^{25}$: –243 (*c* 0.44, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.84 (d, *J* = 10.4 Hz, 1H), 6.69 (s, 1H), 6.53 (s, 1H), 6.14 (dd, *J* = 10.4 Hz, 1.0 Hz, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 2.98–2.84 (m, 2H), 2.91 (dd, *J* = 16.5 Hz, 1.1 Hz, 1H), 2.60–2.54 (m, 1H), 2.56 (d, *J* = 16.5 Hz, 1H), 2.47–2.40 (m, 1H), 2.45 (s, 3H), 2.32–2.22 (m, 1H), 2.07–1.97 (m, 2H), 1.82–1.71 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.8, 150.3, 147.9, 147.1, 135.7, 129.9, 126.3, 111.1, 110.5, 63.1, 56.1, 55.8, 51.6, 49.5, 48.3, 36.2, 33.3, 25.1, 24.6; IR (NaCl/thin film): 2929, 2851, 2832, 2790, 2252, 1681, 1610, 1515, 1464, 1452, 1356, 1255, 1207, 1140, 1068, 1035, 1010, 916, 886, 856, 730; HRMS (EI+) calc'd for $C_{19}H_{24}NO_3$ $[M+H]^+$ 314.1751, found 314.1748.

Preparation of hemiaminal 121.



To a solution of enone **118** (93.8 mg, 0.299 mmol, 1.0 equiv) in THF (3.0 mL) was added *tert*-butylhydroperoxide (TBHP) (214 μL of a 70% aq. solution, 1.50 mmol, 5.0 equiv) and Triton B (110 μL of a 40% solution in methanol, 0.239 mmol, 0.8 equiv) dropwise by syringe, and the solution stirred 17 hours at room temperature. The reaction was then quenched by the addition of a solution of saturated aqueous $Na_2S_2O_3$ (7 mL) and stirred for an additional 30 minutes. H_2O (15 mL) was added, the solution extracted with CH_2Cl_2 (3 x 20 mL). The organic layers combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford a clear oil. The oil was then redissolved in CH_2Cl_2 (2 mL), then loaded onto dry silica gel and allowed to sit for 2 hours. Flash chromatography (60 to 100% EtOAc in hexanes) afforded hemiaminal **121** as a white foam (75.0 mg, 0.228 mmol, 76% yield). $[\alpha]_D^{25}$: –204 (*c* 0.65, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.86 (s, 1H), 6.57 (s, 1H), 6.21 (s, 1H), 4.27 (br s, 1H), 3.85 (s, 3H), 3.85 (s, 3H), 3.02 (ddd, *J* = 12.2, 5.3, 1.6 Hz, 1H), 2.94–2.81 (m, 2H), 2.67–2.57 (m, 2H), 2.46 (td, *J* =12.5, 3.7 Hz, 1H), 2.45 (d, *J* = 12.5 Hz, 1H), 2.28 (td, *J* =13.3, 5.3 Hz, 1H), 2.24 (s, 3H), 2.12 (dd, *J* = 12.5, 2.9 Hz, 1H), 1.70–1.64 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.5, 168.0, 148.2, 147.6, 132.2, 127.2, 124.8, 111.0, 108.5, 83.1, 55.9, 55.8, 49.2, 46.8, 43.5, 36.3, 35.9, 31.2, 29.8; IR (NaCl/thin film): 3468, 2933, 2848, 1666, 1619, 1517, 1465, 1354, 1259, 1228, 1187, 1124, 1089, 1006, 914, 870, 789, 729; HRMS (EI+) calc'd for $C_{19}H_{24}NO_4$ $[M+H]^+$ 330.1700, found 330.1713.

Preparation of cepharatine D (123).



To a solution of hemiaminal **121** (30 mg, 91 μmol, 1.0 equiv) in THF (1.8) mL at –78 °C was added a solution of KHMDS in THF (0.21 mL of a 0.9 M solution in THF, 0.191 mmol, 2.1 equiv). The yellow solution was stirred at –78 °C for 10 minutes, then warmed to 0 °C and stirred for 20 minutes. The solution was again cooled to –78 °C, and a solution of **122** (27.6 mg, 0.128 mmol, 1.4 equiv) in THF (0.25 mL) was added dropwise. After 50 minutes, the solution was quenched with saturated aqueous NH_4Cl (20 mL), warmed to room temperature, and extracted with EtOAc (3 x 20 mL). The organic layers were then combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Flash chromatography (1 to 2 % MeOH in CH_2Cl_2) afforded (–)-cepharatine D (**123**) as a bright yellow foam (18.0 mg, 55.0 μmol, 60% yield). $[\alpha]_D^{25} = -227$ (*c* 0.51, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99 (s, 1H), 6.74 (d, *J* = 9.5 Hz, 1H), 6.72 (s, 1H), 6.32 (d, *J* = 9.3 Hz, 1H), 6.15 (s, 1H), 4.42 (br s, 1H), 3.90 (s, 3H), 3.89 (s, 3H), 2.87 (ddd, *J* = 12.6, 5.1, 1.6 Hz, 1H), 2.75 (d, *J* = 12.2 Hz, 1H), 2.62 (td, *J* = 12.7, 3.7 Hz, 1H), 2.31 (dd, 12.2, 2.9 Hz, 1H), 2.24 (s, 3H), 1.98 (td, *J* = 13.1, 5.1 Hz, 1H), 1.58 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.4, 161.4, 150.3, 147.9, 135.9, 135.5, 124.2, 123.5, 123.2, 111.6, 107.6, 83.0, 56.1, 56.0, 46.8, 56.0, 46.8, 45.0, 43.7, 38.1, 36.0; ^{1}H NMR (500 MHz, CD_3OD) δ 7.07 (s, 1H), 6.90 (s, 1H), 6.84 (d, *J* = 9.3 Hz, 1H), 6.37 (d, *J* = 9.3 Hz, 1H), 6.10 (s, 1H), 3.91 (s, 3H), 3.84 (s, 3H), 2.82 (dd, *J* = 12.7, 4.9 Hz, 1H), 2.68 (d, *J* = 12.2 Hz, 1H), 2.56 (td, *J* = 12.8, 3.5 Hz, 1H), 2.23 (d, *J* = 12.2, 2.8 Hz, 1H), 2.21 (s, 3H), 1.92 (td, *J* = 13.2, 5.1 Hz, 1H), 1.58 – 1.50 (m, 1H); ^{13}C NMR (126 MHz, CD_3OD) δ 194.7, 162.7, 151.8, 149.6, 137.1, 136.9, 126.0, 125.4, 124.1, 113.5, 109.5, 84.7, 56.7, 56.6, 47.9, 46.4, 44.9, 39.0, 36.7; IR (NaCl/thin film): 3455, 2925, 2843, 1732, 1650, 1608, 1554, 1516, 1463, 1376, 1340, 1275, 1235, 1190, 1135, 1081, 877, 784; HRMS (EI+) calc'd for $C_{19}H_{21}NO_4$ $[M+H]^+$ 328.1543, found 330.1552.

Comparison of Spectroscopic Data for Natural[32] and Synthetic (–)-Cepharatine D

^{1}H NMR Data (both spectra are referenced to 3.30 ppm)

Reported[3]	Synthetic
7.06 (s, 1H)	7.07 (s, 1H)
6.89 (s, 1H)	6.90 (s, 1H)
6.84 (d, *J* = 9.2 Hz, 1H)	6.84 (d, *J* = 9.3 Hz, 1H)
6.36 (d, *J* = 9.2 Hz, 1H)	6.37 (d, *J* = 9.3 Hz, 1H)
6.10 (s, 1H)	6.10 (s, 1H)
3.92 (s, 3H)	3.91 (s, 3H)
3.83 (s, 3H)	3.84 (s, 3H)
2.90 (m, 1H)	2.82 (dd, *J* = 12.7, 4.9 Hz, 1H)
2.67 (d, *J* = 12.0 Hz, 1H)	2.68 (d, *J* = 12.2 Hz, 1H)
2.66 (m, 1H)	2.56 (td, *J* = 12.8, 3.5 Hz, 1H)
2.19 (m, 1H)	2.23 (d, *J* = 12.2, 2.8 Hz, 1H)
2.18 (s, 3H)	2.21 (s, 3H)
2.02 (m, 1H)	1.92 (td, *J* = 13.2, 5.1 Hz, 1H)
1.59 (m, 1H)	1.58 – 1.50 (m, 1H)

^{13}C NMR Comparsion Data (both spectra are referenced to 49.0 ppm)

Reported	Synthetic
194.7	194.7
162.7	162.7
151.7	151.8
149.5	149.6
137.0	137.1
136.9	136.9
126.0	126.0
125.3	125.4
124.1	124.1
113.4	113.5
109.3	109.5
84.7	84.7
56.6	56.7
56.5	56.6
47.8	47.9
46.4	46.4
44.8	44.9
39.0	39.0
36.7	36.7

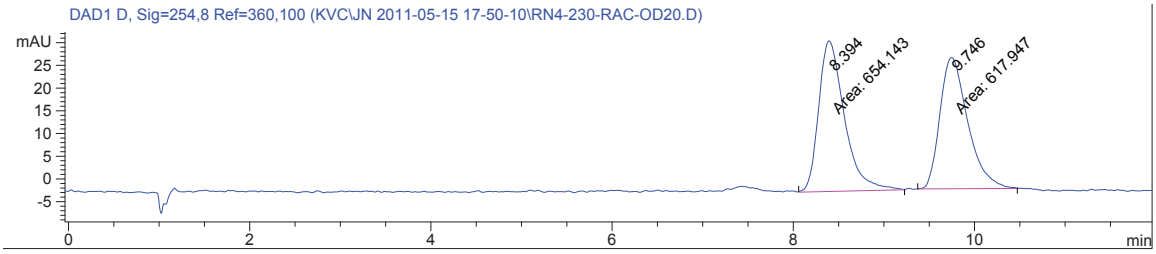
Optical Rotation[33]

Natural	Synthetic
$[\alpha]_D^{17}$: –321 (*c* 1.01, MeOH)	$[\alpha]_D^{17}$: –227 (*c* 0.51, MeOH)

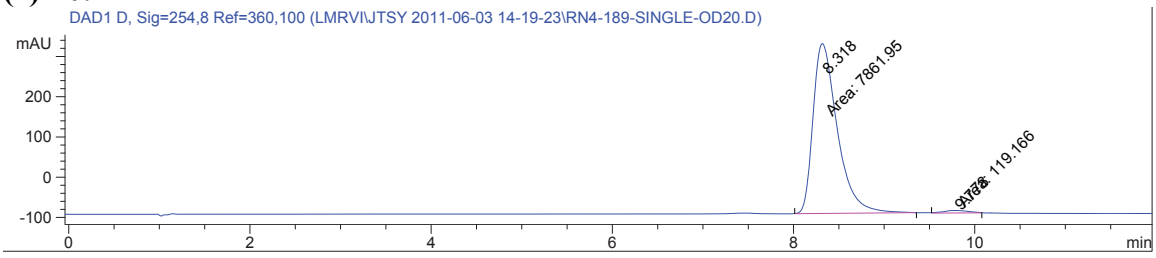
Chiral SFC Traces

Method Information: OD-H column, 20% IPA, 12.0 minutes.

***rac*-10:**

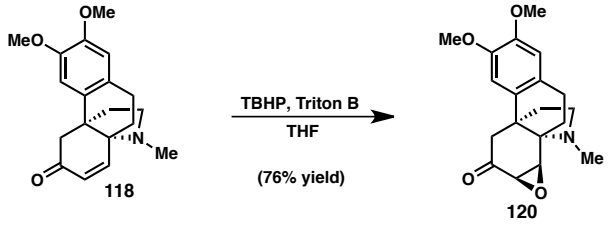


(–)-10:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.318	MM	0.3103	7861.95264	422.33008	98.5069
2	9.778	MM	0.3079	119.16633	6.45073	1.4931
Totals :				7981.11897	428.78081	

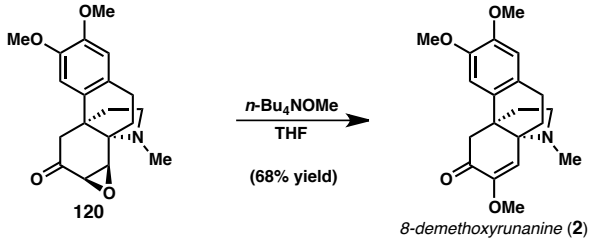
Preparation of epoxyketone 120.



To a solution of enone **118** (62.6 mg, 0.200 mmol, 1.0 equiv) in THF (2.0 mL) was added TBHP (143 μL of a 70% aq. solution, 1.0 mmol, 3.0 equiv) and Triton B (73 μL of a 40% solution in methanol, 0.16 μmmol, 0.8 equiv) dropwise by syringe, and the solution stirred 17 hours at room temperature. The reaction was quenched by the addition of saturated aqueous $Na_2S_2O_3$ (6 mL) and stirred an additional 30 minutes. H_2O (15 mL) was then added, the solution extracted with CH_2Cl_2 (3 x 20 mL), and the organic layers

combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford a clear oil. Flash chromatography (30 to 50% EtOAc in hexanes) on Florisil afforded epoxyketone **120** as a white foam (40.0 mg, 0.075 mmol, 61% yield). $[\alpha]_D^{25}$: +30 (*c* 0.70, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.58 (s, 1H), 6.52 (s, 1H), 3.84 (s, 2H), 3.82 (s, 2H), 3.49 (d, *J* = 3.9 Hz, 1H), 3.32 (dd, *J* = 3.8, 1.0 Hz, 1H), 2.95 (d, *J* = 14.0 Hz, 1H), 2.77 (m, 3H), 2.63 (dt, *J* = 16.0, 3.9 Hz, 1H), 2.56 (s, 3H), 2.50 (dd, *J* = 14.0, 1.0 Hz, 1H), 2.21–2.16 (m, 2H), 2.10 (ddd, *J* = 13.2, 8.0, 5.3 Hz, 1H), 2.01–1.94 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 207.1, 147.8, 147.2, 134.5, 127.4, 110.7, 110.1, 60.5, 60.4, 56.0, 56.0, 55.7, 52.5, 51.4, 45.8, 37.2, 33.3, 24.9, 24.33; IR (NaCl/thin film): 2934, 2833, 2792, 1716, 1610, 1516, 1464, 1454, 1358, 1330, 1256, 1202, 1142, 1070, 1005, 973, 873, 853, 801, 733; HRMS (EI+) calc'd for $C_{19}H_{23}NO_4$ $[M+H]^+$ 330.1700, found 330.1710.

Preparation of 8-Demethoxyrunanine (2).



To epoxyketone **120** (40.8 mg, 0.124 mmol, 1.0 equiv) was added a freshly prepared solution of *n*-Bu_4NOMe[24] (2.5 mL of a 0.5 M solution in THF, 1.2 mmol, 10 equiv) by syringe and the solution was then heated to 50 °C for 11 hours. The reaction was then cooled, diluted with brine (10 mL), and extracted with CH_2Cl_2 (3 x 10 mL). The organic layers were then combined, dried over Na_2SO_4, filtered, and concentrated in vacuo to isolate a brown oil that was purified by flash chromatography (SiO_2 deactivated with 0.5% Et_3N, 40 to 80% EtOAc in Hexanes) to isolate synthetic (–)-8-demethoxyrunanine (**2**) as a white foam (29.1 mg, 84.8 mmol, 68% yield). $[\alpha]_D^{20}$: –185 (*c* 0.51, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.67 (s, 1H), 6.52 (s, 1H), 5.64 (s, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 3.65 (s, 3H), 3.04 (d, *J* = 16.6 Hz, 1H), 2.92 (td, *J* = 9.3, 3.7 Hz, 1H), 2.87 (ddd, *J* = 15.9, 12.8, 4.9 Hz), 2.66 (d, *J* =16.4 Hz, 1H), 2.55 (ddd, *J* = 15.9, 5.0, 2.8 Hz, 1H), 2.44–

2.37 (m, 1H), 2.42 (s, 3H), 2.26 (ddd, J = 13.3, 9.6, 6.2 Hz, 1H), 2.09–1.99 (m, 2H), 1.80 (ddd, J = 13.9, 12.8, 5.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.2, 151.2, 147.9, 147.1, 135.3, 126.4, 114.7, 111.1, 110.6, 63.7, 56.0, 55.8, 55.0, 51.5, 49.6, 48.1, 36.4, 33.5, 26.7, 25.0; IR (NaCl/thin film): 2926, 2848, 2832, 2787, 1693, 1624, 1515, 1463, 1451, 1376, 1356, 1282, 1257, 1217, 1205, 1156, 1136, 1114, 1095, 1066, 1051, 1013, 962, 883, 858, 800, 731, 665 cm^{-1}; HRMS (EI+) calc'd for $C_{20}H_{26}NO_4$ $[M+H]^+$ 344.1856, found 344.1863.

Comparison of Spectroscopic Data for Natural[15] and Synthetic 8-demethoxyrunanine

^{1}H NMR Comparison Data

Reported	Synthetic
6.65 (s, 1H)	6.67 (s, 1H)
6.51 (s, 1H)	6.52 (s, 1H)
5.63 (s, 1H)	5.64 (s, 1H)
3.82 (s, 3H)	3.84 (s, 3H)
3.81 (s, 3H)	3.83 (s, 3H)
3.63 (s, 3H)	3.65 (s, 3H)
3.04 (d, J = 16.4 Hz, 1H)	3.04 (d, J = 16.6 Hz, 1H)
2.84 (m, 1H)	2.92 (td, J = 9.3, 3.7 Hz, 1H)
2.84 (m, 1H)	2.87 (ddd, J = 15.9, 12.8, 4.9 Hz)
2.65 (d, J = 16.4 Hz, 1H)	2.66 (d, J =16.4 Hz, 1H)
2.55 (ddd, J = 16.0, 4.8, 2.8 Hz, 1H)	2.55 (ddd, J = 15.9, 5.0, 2.8 Hz, 1H)
2.41 (s, 3H)	2.42 (s, 3H)
2.39 (m, 1H)	2.44 – 2.37 (m, 1H)
2.25 (m, 1H)	2.26 (ddd, J = 13.3, 9.6, 6.2 Hz, 1H)
2.05 (m, 1H)	2.09 – 1.99 (m, 2H)
2.01 (ddd, J = 14.0, 4.8, 2.8 Hz, 1H)	–
1.79 (ddd, J = 14.0, 13.2, 4.8 Hz, 1H)	1.80 (ddd, J = 13.9, 12.8, 5.1 Hz, 1H)

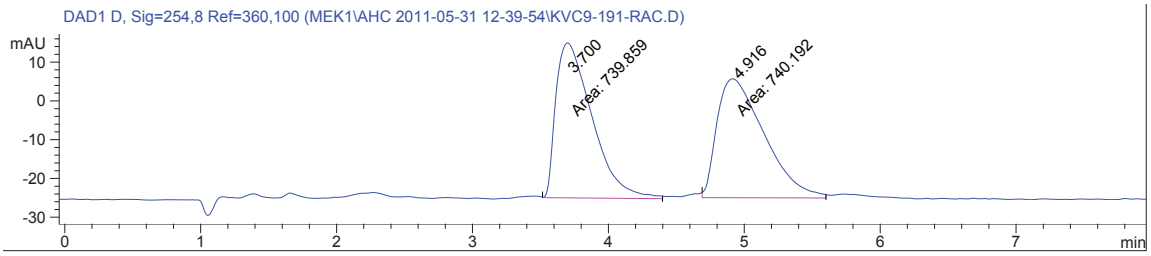
^{13}C NMR Comparison Data

Reported	Synthetic
193.2	193.2
151.1	151.2
147.8	147.9
147.0	147.0
135.2	135.3
126.3	126.4
114.6	114.7
111.0	111.1
110.4	110.6
63.7	63.8
56.0	56.1
55.7	55.8
54.9	55.1
51.4	51.5
49.5	49.7
48.0	48.1
36.3	36.4
33.4	33.5
26.6	26.7
24.8	25.0

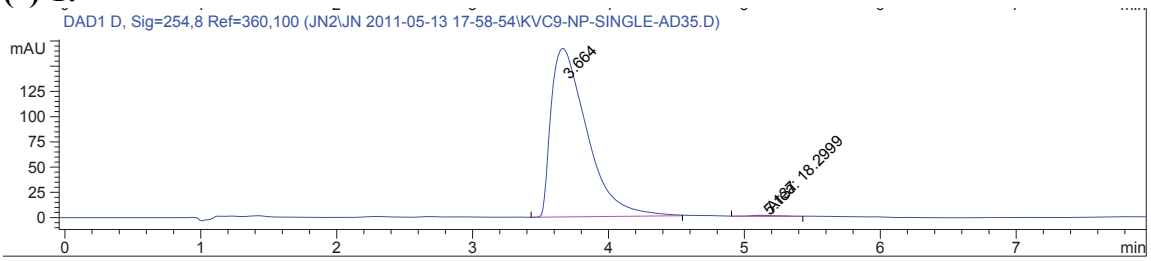
Optical Rotation[34]

Natural	Synthetic
$[\alpha]_D^{20}$: –244 (c 0.48, $CHCl_3$)	$[\alpha]_D^{20}$: –185 (c 0.51, $CHCl_3$)

Chiral SFC Traces:
Method Information:AD column, 35% IPA, 8.0 minutes.
***rac*-1:**



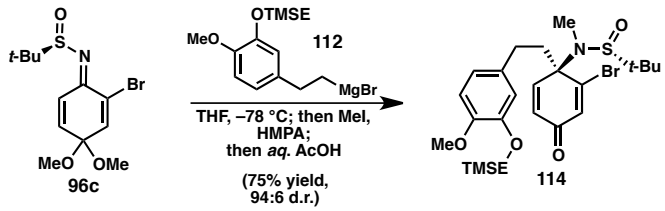
(–)-1:



Signal 2: DAD1 D, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.664	BB	0.2798	3058.54810	166.89442	99.4052
2	5.137	MM	0.2913	18.29991	1.04703	0.5948
Totals :				3076.84801	167.94145	

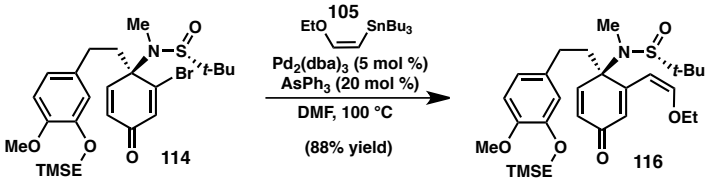
Preparation of sulfinamide 114.



To a solution of bromosulfinimine **96c** (2.49 g, 7.42 mmol) in THF (15 mL) at –78 °C was added a solution of Grignard reagent **112**[35] (0.51M solution in THF, 16.0 mL, 8.16 mmol) dropwise by syringe. The solution was then stirred at –78 °C for one hour, then MeI (1.4 mL, 22 mmol) and HMPA (3.9 mL, 22 mmol) sequentially added dropwise by syringe, and the solution stirred at –78 °C for 10 minutes. The solution was then warmed

to 23 °C and stirred for an additional 2 hours, then quenched by the addition of aqueous AcOH (10% v/v, 30 mL). After 3.5 hours, the mixture was diluted with EtOAc (150 mL), washed with H_2O (3 x 100 mL), and the aqueous layers combined and back extracted with EtOAc (3 x 100 mL). The ethereal layers were then combined, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford a brown oil. The diastereoselectivity was determined by LC/MS: 96:4 d.r. (5→95% MeCN/H_2O, t = 0–10 min, 1 mL/min. Major diastereomer: t_R = 6.7 min, minor diastereomer: t_R = 7.2 min). Flash chromatography (20% to 50% EtOAc in Hexanes) afforded sulfinamide **114** as a white solid foam (3.09 g, 5.55 mmol, 75% yield). $[\alpha]_D^{25}$: +16.9 (*c* 0.92, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.92 (d, *J* = 1.8 Hz, 1H), 6.81 (d, *J* = 10.0 Hz, 1H), 6.77 (d, *J* = 8.2 Hz, 1H), 6.64 (dd, *J* = 8.1, 2.0 Hz, 1H), 6.59 (d, *J* = 2.0 Hz, 1H), 6.43 (dd, *J* = 10.0, 1.8 Hz, 1H), 4.12–4.04 (m, 2H), 3.81 (s, 3H), 2.80 (td, *J* = 12.3, 5.0 Hz, 1H), 2.46 (s, 3H), 2.38–2.22 (m, 2H), 1.84 (td, *J* = 12.4, 5.2 Hz, 1H), 1.21 (s, 9H), 1.21–1.16 (m, 2H), 0.07 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 183.1, 150.7, 150.1, 148.3, 148.2, 136.4, 132.2, 129.6, 120.0, 113.4, 111.7, 68.8, 66.3, 59.2, 55.9, 38.2, 29.8, 26.7, 24.2, 17.8, –1.4; IR (NaCl/thin film): 3045, 2951, 2900, 2866, 2834, 1670, 1640, 1592, 1515, 1463, 1455, 1442, 1425, 1360, 1292, 1253, 1236, 1156, 1137, 1079, 1055, 1032, 950, 886, 859, 839, 786; HRMS (EI+) calc'd for $C_{25}H_{38}BrNO_4SSi$ $[M+Na]^+$ 578.1366, found 578.1555.

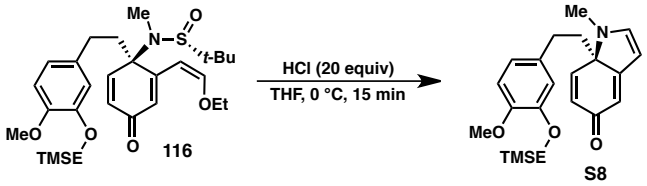
Preparation of enol ether 116.



To a solution of sulfinamide **114** (1.28 g, 2.30 mmol) in DMF (19 mL) was added $Pd_2(dba)_3$ (105 mg, 0.115 mmol), $AsPh_3$ (141 mg, 0.460 mmol), and stannane **105** (0.84 mL, 2.53 mmol). The solution was degassed with N_2 for 30 minutes, then heated and stirred at 100 °C for 1 hour. Upon cooling to room temperature, the solution was passed through a short plug of Celite, diluted with EtOAc (200 mL), and washed with H_2O (3 x 100 mL). The aqueous layers were combined and back extracted with EtOAc (3 x 75

mL), then the organic layers combined, washed with brine (250 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford a light brown oil. Flash chromatography (50% to 100% EtOAc in hexanes) afforded **116** (>10:1 mixture of *Z:E*-isomers by ^{1}H NMR) as a tan solid (1.11 g, 88% yield). $[\alpha]_D^{25}$: –66 (*c* 1.34, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.19 (d, *J* = 2.0 Hz, 1H), 6.76 (d, *J* = 8.3 Hz, 1H), 6.61 (d, *J* = 7.1 Hz, 1H), 6.59 (dd, *J* = 8.1, 2.0 Hz, 1H), 6.55 (d, *J* = 10.0 Hz, 1H), 6.55 (d, *J* = 2.2 Hz, 1H), 6.38 (dd, *J* = 10.0, 2.0 Hz, 1H), 5.17 (d, *J* = 7.3 Hz, 1H), 4.09–4.02 (m, 4H), 3.81 (s, 3H), 2.51 (ddd, *J* = 12.7, 10.3, 7.1 Hz, 1H), 2.45 (s, 3H), 2.33–2.26 (m, 2H), 1.90–1.80 (m, 1H), 1.35 (t, *J* = 7.08 Hz, 3H), 1.24 (s, 9H), 1.21–1.16 (m, 2H), 0.07 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 186.7, 154.8, 153.6, 149.5, 148.2, 148.0, 133.2, 130.5, 128.8, 119.9, 113.5, 111.6, 98.8, 70.7, 66.6, 66.3, 58.9, 55.9, 38.3, 29.9, 27.1, 24.4, 17.8, 15.4, –1.4; IR (NaCl/thin film): 2952, 2899, 2834, 1661, 1623, 1576, 1515, 1453, 1384, 1302, 1258, 1157, 1137, 1099, 1055, 957, 896, 859, 839, 803, 767 cm^{-1}; HRMS (EI+) calc'd for $C_{29}H_{45}NO_5SSi$ $[M+H]^+$ 547.2860, found 548.2850.

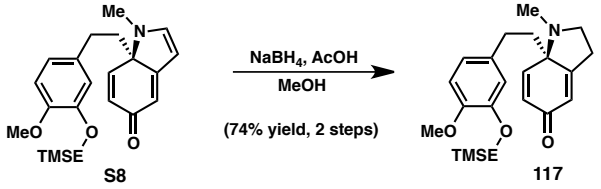
Preparation of Enamine S8.



To a solution of enol ether **116** (702 mg, 1.28 mmol) in THF (12.8 mL) at 0 °C was added a solution of HCl (2.0 M solution in Et_2O, 12.8 mL, 25.6 mmol) dropwise by syringe over 1 minute. The reaction was allowed to stir 15 minutes at 0 °C and then quenched by the addition of aqueous KOH (10% w/v, 13 mL), and stirred for an additional 5 minutes. The mixture was then diluted with H_2O (50 mL), and extracted with EtOAc (3 x 50 mL). The organic layers were then combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to isolate a bright red foam. Column chromatography (2% MeOH in CH_2Cl_2) afforded a red foam of adequate purity for the next step. $[\alpha]_D^{25}$: –1185 (*c* 0.22, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.99 (dd, *J* = 9.7, 0.5 Hz, 1H), 6.89 (d, *J* = 3.17 Hz, 1H), 6.74 (d, *J* = 8.3 Hz, 1H), 6.59 (d, *J* = 8.1, 2.2

Hz, 1H), 6.55 (d, J = 2.0 Hz, 1H), 6.18 (dd, J = 9.9, 1.6 Hz, 1H), 5.91 (d, J = 1.5 Hz, 1H), 5.49 (dd, J = 3.3, 0.6 Hz, 1H), 4.08–4.04 (m, 2H), 3.81 (s, 3H), 3.05 (s, 1H), 2.42–2.31 (m, 2H), 2.11–1.99 (m, 2H), 1.19–1.16 (m, 2H), 0.08 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 184.8, 174.5, 153.3, 148.3, 148.0, 140.1, 132.8, 131.2, 120.0, 113.6, 111.7, 110.0, 99.7, 72.7, 66.4, 56.0, 45.7, 31.6, 29.1, 17.9, –1.4; IR (NaCl/thin film): 2951, 2916, 1631, 1569, 1514, 1424, 1248, 1157, 1137, 1108, 108, 1050, 1032, 859, 837, 649; HRMS (EI+) calc'd for $C_{23}H_{31}NO_3Si$ $[M+H]^+$ 398.2146, found 398.2149.

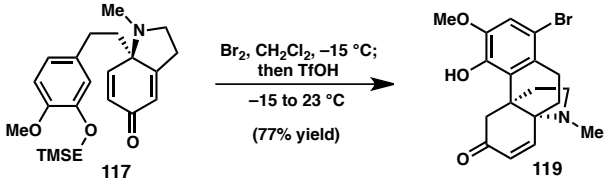
Preparation of dihydroindolone 117.



To a solution of enamine **S8** in MeOH (26 mL) at 23 °C was added a solution of $NaBH_4$ (97 mg, 2.56 mmol) in AcOH (9.8 mL), dropwise by syringe. The solution was stirred at 20 °C for 1 hour, then a second portion of $NaBH_4$ (97 mg, 2.56 mmol) in AcOH (9.8 mL) was added and stirring was continued for an additional hour. The reaction was cooled to 0 °C in an ice/water bath and neutralized by the slow addition of aqueous KOH (30% w/v, 65 mL). The solution was then diluted with H_2O (50 mL) and extracted with EtOAc (3 x 100 mL). The combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by flash chromatography (2% MeOH in CH_2Cl_2) to afford dihydroindolone **117** as a yellow oil (379 mg, 0.948 mmol, 77% yield over two steps). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.98 (d, J = 10.0 Hz, 1H), 6.76 (d, J = 8.1 Hz, 1H), 6.61 (dd, J = 8.1, 2.0 Hz, 1H), 6.56 (d, J = 1.7 Hz, 1H), 6.34 (dd, J = 10.0, 1.5 Hz, 1H), 6.20 (app d, J = 1.7 Hz, 1H), 4.10–4.05 (m, 2H), 3.82 (s, 3H), 3.18 (ddd, J = 10.5, 8.5, 4.2 Hz, 1H), 3.05 (td, J = 10.0, 7.0 Hz, 1H), 2.79–2.68 (m, 2H), 2.42 (s, 3H), 2.36 (ddd, J = 13.9, 10.7, 6.4 Hz, 1H), 2.22 (ddd, J = 14.0, 10.9, 6.5 Hz, 1H), 1.90–1.81 (m, 2H), 1.22–1.17 (m, 2H), 0.08 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 186.7, 167.0, 148.2, 147.9, 146.0, 133.5, 130.2, 123.3, 119.8, 113.4, 111.6, 66.6, 66.3, 56.0, 51.6, 36.5, 32.0, 29.6, 27.8, 17.9, –1.4; IR (NaCl/thin film): 2949, 2850, 1669, 1644, 1606, 1589,

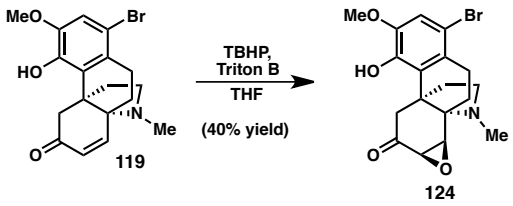
1514, 1442, 1424, 1305, 1253, 1234, 1176, 1150, 1137, 1032, 1013, 942, 890, 859, 839, 695; HRMS (EI+) calc'd for $C_{23}H_{33}NO_3Si$ $[M+H]^+$ 400.2302, found 400.2283.

Preparation of propellane 119.



To a solution of dihydroindolone **117** (414 mg, 1.04 mmol) in CH_2Cl_2 (21 mL) at –15 °C was added Br_2 (80 μL, 1.55 mmol) dropwise by syringe. The solution was stirred for 20 minutes, then TfOH (550 μL, 6.22 mmol) was added dropwise by syringe and the solution was warmed to room temperature. After 12 minutes, the reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (50 mL), diluted with CH_2Cl_2 (60 mL), and washed with aqueous $NaHCO_3$ (2 x 100 mL). The aqueous layers were extracted with CH_2Cl_2 (100 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford a light brown foam. Flash chromatography (20 to 30% EtOAc in hexanes) afforded propellane **119** as an off-white solid (302 mg, 0.798 mmol, 77% yield). $[\alpha]_D^{25}$: –226 (*c* 0.42, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.98 (s, 1H), 6.82 (d, *J* = 10.3 Hz, 1H), 6.15 (dd, *J* = 10.4, 1.1 Hz, 1H), 5.95 (s, 1H), 3.86 (s, 3H), 3.62 (dd, *J* = 16.6, 1.2 Hz, 1H), 2.89–2.81 (m, 2H), 2.69–2.55 (m, 2H), 2.44 (s, 3H), 2.41–2.36 (m, 1H), 2.04–1.96 (m, 2H), 1.77–1.69 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 199.3, 149.7, 145.4, 143.2, 130.8, 130.2, 127.4, 114.0, 112.9, 63.2, 56.4, 51.6, 48.0, 43.8, 33.4, 33.2, 25.8, 24.8; IR (NaCl/thin film): 3338, 2926, 2850, 2790, 1673, 1601, 1470, 1436, 1420, 1388, 1357, 1314, 1314, 1276, 1235, 1125, 1064, 1038, 879, 785. HRMS (EI+) calc'd for $C_{18}H_{20}BrNO_3$ $[M+H]^+$ 378.0699, found 378.0683.

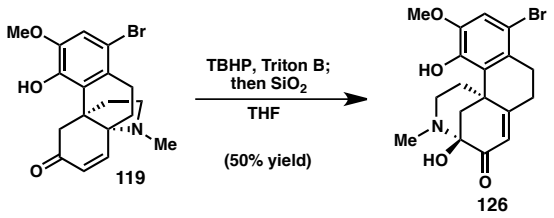
Preparation of epoxyketone 124.



To a solution of enone **119** (13.3 mg, 0.035 mmol) in THF (0.70 mL) at 28 °C was added TBHP (100 μL of a 5.5M solution in decane, 0.550 mmol) and Triton B (0.05 mL of a 40% solution in methanol, 105 μmol) dropwise by syringe, and the solution stirred for 16 hours at 28 °C. The reaction was quenched by the addition of saturated aqueous - $Na_2S_2O_3$ (2 mL) and stirred for an additional 30 minutes. H_2O (10 mL) was added, and the solution was extracted with CH_2Cl_2 (3 x 15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford a clear oil. Flash chromatography (1 to 2% MeOH in CH_2Cl_2) on Florisil afforded epoxyketone **124** as a white foam (5.3 mg, 0.014 mmol, 40% yield). $[\alpha]^{25}_D$: –11 (*c* 0.24, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.97 (s, 1H), 5.93 (s, 1H), 3.84 (s, 3H), 3.51 (d, *J* = 3.91 Hz, 1H), 3.29 (dd, *J* = 3.91, 1.0 Hz, 1H), 3.21 (dd, *J* = 14.2, 1.0 Hz, 1H), 2.95–2.81 (m, 2H), 2.74–2.64 (m, 1H), 2.67 (d, *J* = 13.9 Hz, 1H), 2.58 (ddd, *J* = 16.6, 11.8, 6.3 Hz, 1H), 2.51 (s, 3H), 2.42 (ddd, *J* = 14.4, 9.3, 6.8 Hz), 2.20–2.09 (m, 2H), 2.06–1.96 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 207.4, 145.3, 142.8, 130.3, 127.8, 113.9, 113.0, 60.7, 59.2, 56.4, 55.6, 51.8, 51.4, 40.3, 34.0, 33.3, 25.7, 23.2; IR (NaCl/thin film): 3420, 2937, 2791, 1717, 1603, 1470, 1436, 1356, 1313, 1277, 1238, 876 cm^{-1}; HRMS (EI+) calc'd for $C_{18}H_{20}BrNO_4$ $[M+H]^+$ 394.0648, found 394.0632.

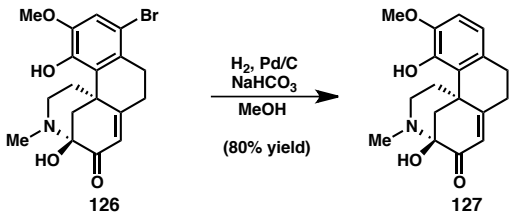
Longer reaction times resulted in higher conversion, but led to oxidative rearrangement of the desired epoxide into an unidentified lactone side product: ^{1}H NMR (300 MHz, $CDCl_3$): 6.99 (s, 1H), 4.44 (d, *J* = 1.9 Hz, 1H), 3.83 (s, 3H), 3.04–2.83 (m, 5H), 2.83–2.64 (m, 3H), 2.36 (s, 3H), 2.20 (ddd, *J* = 18.4, 12.7, 4.0 Hz, 3H), 2.04–1.80 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 176.4, 145.2, 142.1, 130.1, 127.1, 115.0, 114.0, 85.0, 80.4, 73.9, 56.3, 55.6, 54.4, 41.9, 34.2, 27.3, 23.7; IR (NaCl/thin film): 3351, 2930, 2849, 2791, 1784, 1605, 1470, 1434, 1292, 1274; HRMS (EI+) calc'd for $C_{18}H_{20}BrNO_5$ $[M+H]^+$ 410.0598, found 410.0599.

Preparation of hemiaminal 126.



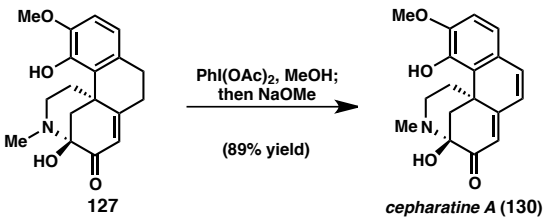
To a solution of enone **119** (106 mg, 0.279 mmol) in THF (5.6 mL) was added TBHP (1.01 mL of a 5.5M solution, 5.58 mmol) and Triton B (0.64 mL of a 40% solution in MeOH, 1.40 mmol) dropwise by syringe, and the solution stirred for 18.5 hours. The reaction was quenched by the addition of saturated aqueous $Na_2S_2O_3$ (10 mL) and saturated NH_4Cl (5 mL), and stirred for an additional 30 minutes. The solution was extracted with CH_2Cl_2 (3 x 30 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford a clear oil. The oil was then redissolved in CH_2Cl_2 and concentrated onto dry SiO_2 and allowed to sit for 2 hours. Flash chromatography (1 to 4% MeOH in CH_2Cl_2) afforded hemiaminal **126** as a light yellow foam (55.2 mg, 0.140, 50% yield). $[\alpha]_D^{25} = -179$ (*c* 0.79, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.01 (s, 1H), 6.19 (br s, 1H), 6.16 (d, *J* = 1.3 Hz, 1H), 4.17 (br s, 1H), 3.88 (s, 3H), 3.42 (d, *J* = 12.7 Hz, 1H), 3.36 (td, *J* = 13.2, 5.6 Hz, 1H), 3.28–3.21 (m, 1H), 3.01 (ddd, *J* = 12.2, 5.5, 1.4 Hz, 1H), 2.65–2.53 (m, 2H), 2.52–2.43 (m, 2H), 2.21 (s, 3H), 1.91 (dd, *J* = 12.7, 2.7 Hz, 1H), 1.42 (dddd, *J* = 13.5, 4.1, 2.6, 1.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 194.8, 167.6, 145.9, 144.1, 128.4, 127.2, 123.8, 113.7, 113.6, 83.2, 77.3, 77.0, 76.8, 56.4, 49.1, 44.8, 42.0, 36.1, 31.7, 31.1, 29.1; IR (NaCl/thin film): 3447, 2929, 2841, 1665, 1599, 1471, 1436, 1275, 1234, 1179, 1-83, 1035, 885; HRMS (EI+) calc'd for $C_{18}H_{20}BrNO_4$ $[M+H]^+$ 394.0648, found 330.0649.

Preparation of dihydrocepharatine A (127).



To a solution of hemiaminal **126** (32.8 mg, 0.083 mmol) in MeOH (0.83 mL) was added solid $NaHCO_3$ (42 mg, 0.50 mmol) and Pd/C (3.2 mg of 10 wt % Pd on activated carbon). The solution was placed under an atmosphere of H_2 and the stirred for 1.5 hours at room temperature. The reaction was diluted with EtOAc, filtered through a plug of Celite, and concentrated under reduced pressure to isolate a yellow oil. Flash chromatography (1 to 4% MeOH in CH_2Cl_2) afforded hemiaminal **127** as a white foam (20.8 mg, 0.066 mmol, 80% yield). $[\alpha]_D^{25} = -284$ (*c* 0.21, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.73 (d, *J* = 8.3 Hz, 1H), 6.61 (app d, *J* = 8.3 Hz, 1H), 6.19 (br s, 1H), 6.15 (d, *J* = 1.2 Hz, 1H), 4.18 (br s, 1H), 3.88 (s, 2H), 3.44 (d, *J* = 12.7 Hz, 1H), 3.34 (td, *J* = 13.2, 5.6 Hz, 1H), 3.01 (ddd, *J* = 12.2, 5.5, 1.4 Hz, 1H), 2.97–2.90 (m, 1H), 2.61–2.42 (m, 3H), 2.22 (s, 3H), 1.99 (dd, *J* = 12.7, 2.7 Hz, 1H), 1.41 (dddd, *J* = 13.5, 4.1, 2.7, 1.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.1, 168.7, 145.6, 144.5, 129.4, 125.5, 124.0, 119.3, 109.1, 83.3, 77.3, 77.0, 76.8, 56.2, 49.2, 44.5, 42.2, 36.1, 31.7, 31.1, 29.3; IR (NaCl/thin film): 3469, 2934, 2842, 2801, 1664, 1484, 1440, 1277, 1234, 1189, 1079, 965; HRMS (EI+) calc'd for $C_{18}H_{21}NO_4$ $[M+H]^+$ 316.1543, found 316.1541.

Preparation of cepharatine A (130).



To a solution of hemiaminal **127** (14.1 mg, 44.8 μmol) in MeOH (0.89 mL) at 0 °C was added a solution of $PhI(OAc)_2$ (15.1 mg, 47 μmol, 1.05 equiv) dropwise by syringe. The solution was stirred for 20 minutes before a solution of NaOMe (0.5 M in MeOH, 0.224 mmol, 5.0 equiv) was added dropwise by syringe. After 5 minutes, the reaction was warmed to room temperature, stirred for 20 minutes, then quenched with saturated aqueous NH_4Cl (5 mL). The reaction was diluted with H_2O, extracted with EtOAc (3 x 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford a yellow-orange oil. Flash chromatography on silica gel (1 to 3% MeOH in CH_2Cl_2) afforded **130** (12.5 mg, 40.0 μmol, 89% yield) as a yellow-

orange foam. $[\alpha]^{15}_{D} = -537$ (*c* 0.38, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 6.78 (d, *J* = 8.3 Hz, 1H), 6.76 (d, *J* = 8.3 Hz, 1H), 6.70 (d, *J* = 9.3 Hz, 1H), 6.29 (d, *J* = 9.3 Hz, 1H), 6.28 (br s, 1H), 6.12 (s, 1H), 4.29 (br s, 1H), 3.93 (s, 3H), 3.91 (d, *J* = 13.0 Hz, 1H), 2.91–2.84 (m,1H), 2.74–2.58 (m, 2H), 2.24 (s, 3H), 2.22 (dd, *J* = 13.0 Hz, 1H), 1.38 (ddd, *J* = 6.1, 4.7, 2.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 194.1, 161.4, 148.1, 144.4, 136.0, 125.6, 125.5, 124.1, 123.4, 121.3, 108.7, 83.2, 56.2, 46.6, 44.4, 43.5, 36.2, 31.2; IR (NaCl/thin film): 3447, 2929, 2839, 1648, 1609, 1563, 1483, 1440, 1273, 1239, 1192, 1272, 1075, 969 cm^{-1}; HRMS (EI+) calc'd for $C_{18}H_{19}NO_4$ $[M+H]^+$ 314.1387, found 314.1393.

Comparison of Spectroscopic Data for Natural and Synthetic[36] (–)-Cepharatine A

^{1}H NMR Data (both spectra are referenced to 7.27 ppm)

Reported	Synthetic
6.79 (d, *J* = 8.4 Hz, 1H)	δ 6.79 (d, *J* = 8.2 Hz, 1H),
6.77 (d, *J* = 8.4 Hz, 1H)	6.77 (d, *J* = 8.2 Hz, 1H)
6.71 (d, *J* = 9.6 Hz, 1H)	6.71 (d, *J* = 9.3 Hz, 1H)
6.29 (d, *J* = 9.6 Hz, 1H)	6.30 (d, *J* = 9.4 Hz, 1H)
-	6.29 (br s, 1H)
6.13 (s, 1H)	6.13 (s, 1H)
4.32 (br s, 1H)	4.30 (br s, 1H)
3.94 (s, 3H)	3.94 (s, 3H)
3.95 (d, *J* = 12.8 Hz, 1H)	3.92 (d, *J* = 13.0 Hz, 1H)
2.90 (m, 1H)	2.92 – 2.85 (m, 1H)
2.74 (m, 1H)	2.75 – 2.59 (m, 2H)
2.66 (m, 1H)	-
2.25	2.25 (s, 3H)
2.19 (m, 1H)	2.23 (dd, *J* = 13.0, 2.7 Hz, 1H),
1.40 (m, 1H)	1.38 (ddd, *J* = 6.1, 4.7, 2.2 Hz, 1H)

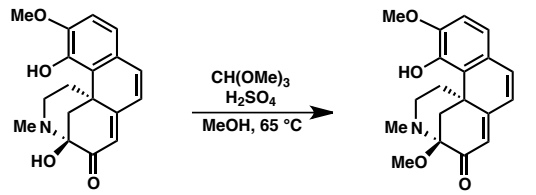
^{13}C NMR Comparsion Data (referenced to 77.0 ppm)

Reported	Synthetic
194.0	194.1
161.6	161.4
148.1	148.1
144.4	144.4
136.1	136.0
125.5	125.6
125.4	125.5
124.0	124.1
123.3	123.4
121.2	121.3
108.7	108.7
83.2	83.2
56.1	56.2
46.6	46.6
44.3	44.4
43.4	43.5
36.2	36.2
31.1	31.2

Optical Rotation

Natural	Synthetic
$[\alpha]^{15}_{D}$: –716 (*c* 0.98, $CHCl_3$)	$[\alpha]^{15}_{D}$ = –537 (*c* 0.38, $CHCl_3$)

Preparation of cepharatine C (131).



cepharatine A (130) *cepharatine C* (131)

To a solution of cepharatine A (7.5 mg, 23.0 μmol mmol) in MeOH (0.46 mL) was added trimethyl orthoformate (0.05 mL) and H_2SO_4 (0.050 mL of a 1M solution in methanol). The solution was then stirred for 1 hour at 65 °C, cooled to room temperature, then slowly quenched with saturated aqueous $NaHCO_3$ (3 mL). The reaction was extracted with EtOAc (4 x 3 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to isolate a yellow oil. Flash chromatography (0.5 to 4% MeOH in CH_2Cl_2) afforded cepharatine C (**131**) as a yellow-orange foam (7.4 mg, 22.6 μmol, 99% yield). $[\alpha]^{16}_D$ = –550 (*c* 0.38, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.78 (d, *J* = 8.2 Hz, 1H), 6.76 (d, *J* = 8.2 Hz, 1H), 6.65 (d, *J* = 9.3 Hz, 1H), 6.26 (t, *J* = 4.7 Hz, 1H), 6.26 (s, 1H), 6.07 (s, 1H), 3.94 (d, *J* = 12.5 Hz, 1H), 3.94 (s, 3H), 3.38 (s, 3H), 2.90–2.81 (m, 1H), 2.64–2.53 (m, 1H), 2.20 (s, 1H), 2.15 (dd, *J* = 12.4, 2.6 Hz, 1H), 1.44–1.34 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.7, 158,0, 147.8, 144.2, 135.0, 126.7, 125.9, 125.5, 123.6, 121.1, 108.7, 87.4, 56.2, 48.6, 46.6, 43.7, 38.8, 36.6, 31.3; ^{1}H NMR (300 MHz, CD_3OD): δ 6.88 (d, *J* = 8.4 Hz, 1H), 6.79 (d, *J* = 8.2 Hz, 1H), 6.76 (d, *J* = 9.4 Hz, 1H), 6.30 (d, *J* = 9.5 Hz, 1H), 6.02 (s, 1H), 4.14 (d, *J* = 12.5 Hz, 1H), 3.89 (s, 3H), 3.31 (s, 3H), 2.83 (ddd, *J* = 11.7, 4.8, 1.6 Hz, 1H), 2.66 (td, *J* = 12.8, 4.8 Hz, 1H), 2.51 (ddd, *J* = 12.9, 11.6, 3.4 Hz, 1H), 2.10 (s, 3H), 2.02 (dd, *J* = 12.5, 1.3 Hz, 1H), 1.34–1.27 (m, 1H); ^{13}C NMR (126 MHz, CD_3OD): δ 193.4, 162.6, 150.8, 146.4, 137.9, 126.8, 126.7, 126.5, 123.7, 122.6, 110.5, 88.9, 56.6, 47.7, 45.4, 40.2, 36.9, 32.0; IR (NaCl/thin film): 3338, 2923, 2849, 1658, 1612, 1566, 1483, 1440, 1296, 1274, 1083, 1022, 878 cm^{-1}; HRMS (EI+) calc'd for $C_{19}H_{21}NO_4$ $[M+H]^+$ 328.1543, found 330.1546.

Comparison of Spectroscopic Data for Natural and Synthetic (–)-Cepharatine C

^{1}H NMR Data (both spectra are referenced to 3.30 ppm)

Reported	Synthetic
6.88 (d, *J* = 8.4 Hz, 1H)	6.88 (d, *J* = 8.4 Hz, 1H)
6.80 (d, *J* = 9.2 Hz, 1H)	6.79 (d, *J* = 8.2 Hz, 1H)
6.77 (d, *J* = 8.4 Hz, 1H)	6.76 (d, *J* = 9.4 Hz, 1H)
6.30 (d, *J* = 9.2 Hz, 1H)	6.30 (d, *J* = 9.5 Hz, 1H)
6.03 (s, 1H)	6.02 (s, 1H)
4.14 (d, *J* = 12.4 Hz, 1H)	4.14 (d, *J* = 12.5 Hz, 1H)
3.90 (s, 3H)	3.89 (s, 3H)
3.31 (s, 3H)	3.31 (s, 3H)
2.85 (m, 1H)	2.83 (ddd, *J* = 11.7, 4.8, 1.6 Hz, 1H)
2.69 (m, 1H)	2.66 (td, *J* = 12.8, 4.8 Hz, 1H)
2.55 (m, 1H)	2.51 (ddd, *J* = 12.9, 11.6, 3.4 Hz, 1H)
2.10 (s, 3H)	2.10 (s, 3H)
2.02 (m, 1H)	2.02 (dd, *J* = 12.5, 1.3 Hz, 1H)
1.29 (m, 1H)	1.34 – 1.27 (m, 1H)

^{13}C NMR Comparsion Data (both spectra are referenced to 49.0 ppm)

Reported	Synthetic
193.6	193.5
162.7	162.6
150.8	150.8
146.5	146.5
137.9	137.9
126.8	126.8
126.7	126.7
126.4	126.5
123.7	123.7
122.6	122.6
110.4	110.5
88.8	88.9
56.6	56.6
49.0	–[37]
47.7	47.7
45.4	45.4
40.1	40.2
36.9	36.9
32.0	32.0

Optical Rotation

Natural	Synthetic
$[\alpha]^{20}_{D}$: –332 (*c* 1.01, MeOH)	$[\alpha]^{15}_{D}$ = –550 (*c* 0.56, MeOH)

2.5. Notes and References

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(23) All other reaction conditions screened provided hemiaminal **121** as the major product or led to significant decomposition.

(24) Di Bussolo, V.; Caselli, M.; Romano, M. R.; Pineschi, M.; Crotti, P. *J. Org. Chem.* **2004**, *69*, 8702–8708.

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(27) Brown, H. C.; Subrahmanyam, C.; Hamaoka, T.; Ravindran, N.; Bowman, D. H.; Misumi, S.; Unni, M. K.; Somayaji, V.; Bhat, N. G. *J. Org. Chem.* **1989**, *54*, 6068–6075.

(28) The product isolated contained <2% minor diastereomer and 3% cis addition

product.

(29) Liu, H.; Tomooka, C. S.; Xu, S. L.; Yerxa, B. R.; Sullivan, R. W.; Xiong, Y.; Moore, H. W. *Org. Synth.* **1999**, *76*, 189.

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(31) To a suspension of Mg turnings (239 mg, 9.8 mmol) in THF (1 mL) was added DIBAL-H (1 mol %). The resulting suspension was heated to reflux, and a solution of 3,4-dimethoxyphenethyl bromide (1 g, 4.1 mmol) in THF (4 mL) was added dropwise. The reaction was maintained at reflux for 1.5 hrs, then cooled to room temperature and used for the sulfinimine addition reaction.

(32) ^{1}H NMR data for cepharatine D was found to be inconsistent with the spectral data provided in the isolation paper. See ref. 21.

(33) It was noted that synthetic (–)-cepharatine D produced a significantly lower specific rotation than reported by the isolation paper. To eliminate the possibility of racemization during the reaction sequence, racemic **123** was synthesized using racemic *tert*-butylsulfinamide by an identical sequence, and the enantiomeric excess of synthetic **123** was determined to be > 98% ee by chiral SFC (see Chiral SFC Traces).

(34) It was noted that synthetic (–)-8-demethoxyrunanine produced a significantly lower specific rotation than reported by the isolation paper. Racemic **2** was synthesized using racemic *tert*-butylsulfinamide*;* the enantiomeric excess of synthetic **2** was determined to be > 98% ee by chiral SFC.

(35) Grignard reagent **112** was prepared in analogy to 3,4-dimethoxyphenethyl)magnesium bromide. See ref. 31.

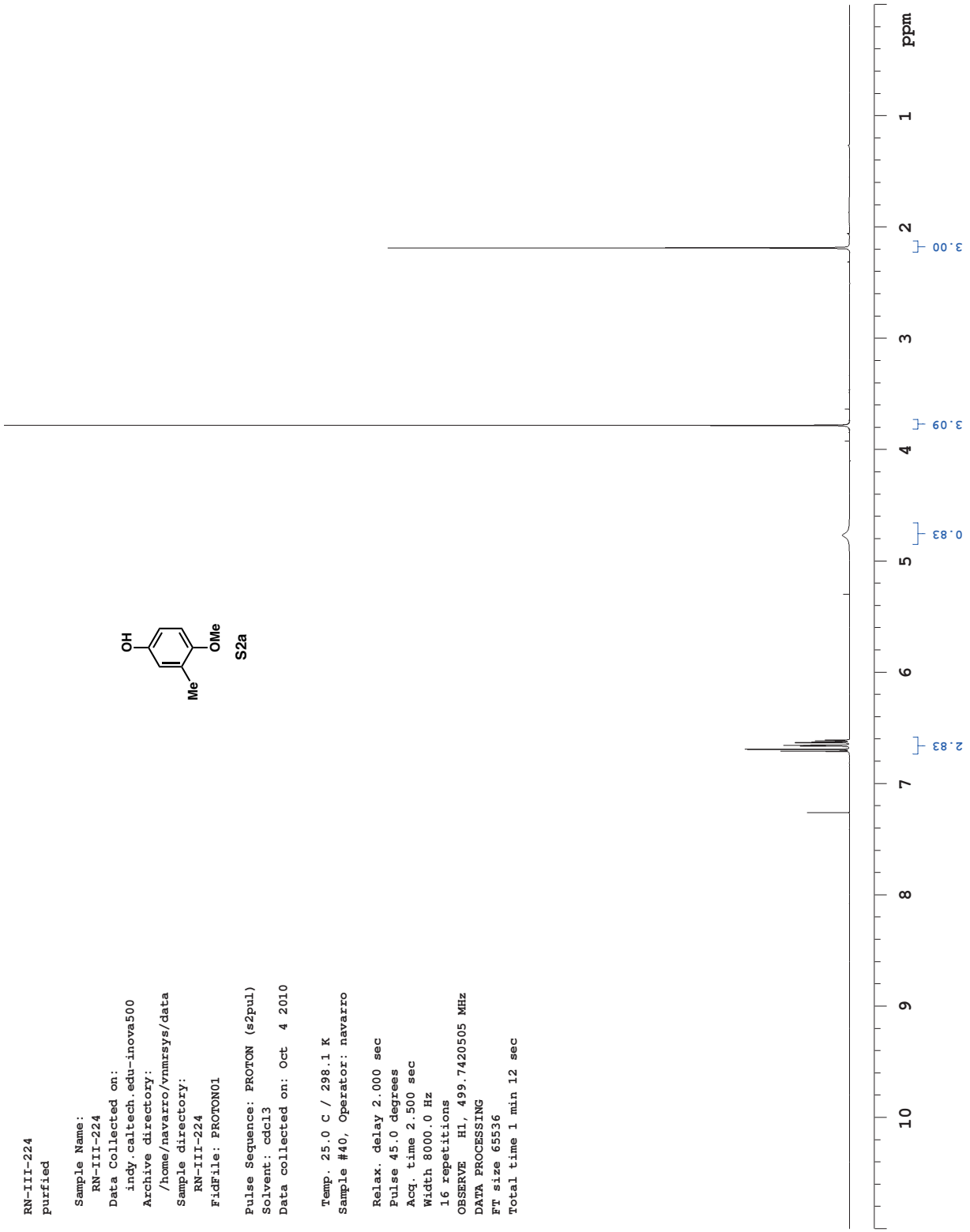
(36) It was noted that synthetic (–)-cepharatine A produced a lower specific rotation than that reported. It is inferred, based on the total syntheses of 8-demethoxyrunanine and cepharatine D, that the lower observed rotation does not necessarily imply any loss of enantiomeric excess.

(37) The corresponding resonance is obscured by the residual solvent peak. Acquisition in $CDCl_3$ shows the analogous signal at δ 48.6 ppm.

APPENDIX 1

Spectra Relevant to Chapter 2:

Development of a Diastereoselective 1,2-Addition to Sulfinyl Imines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Archive directory:
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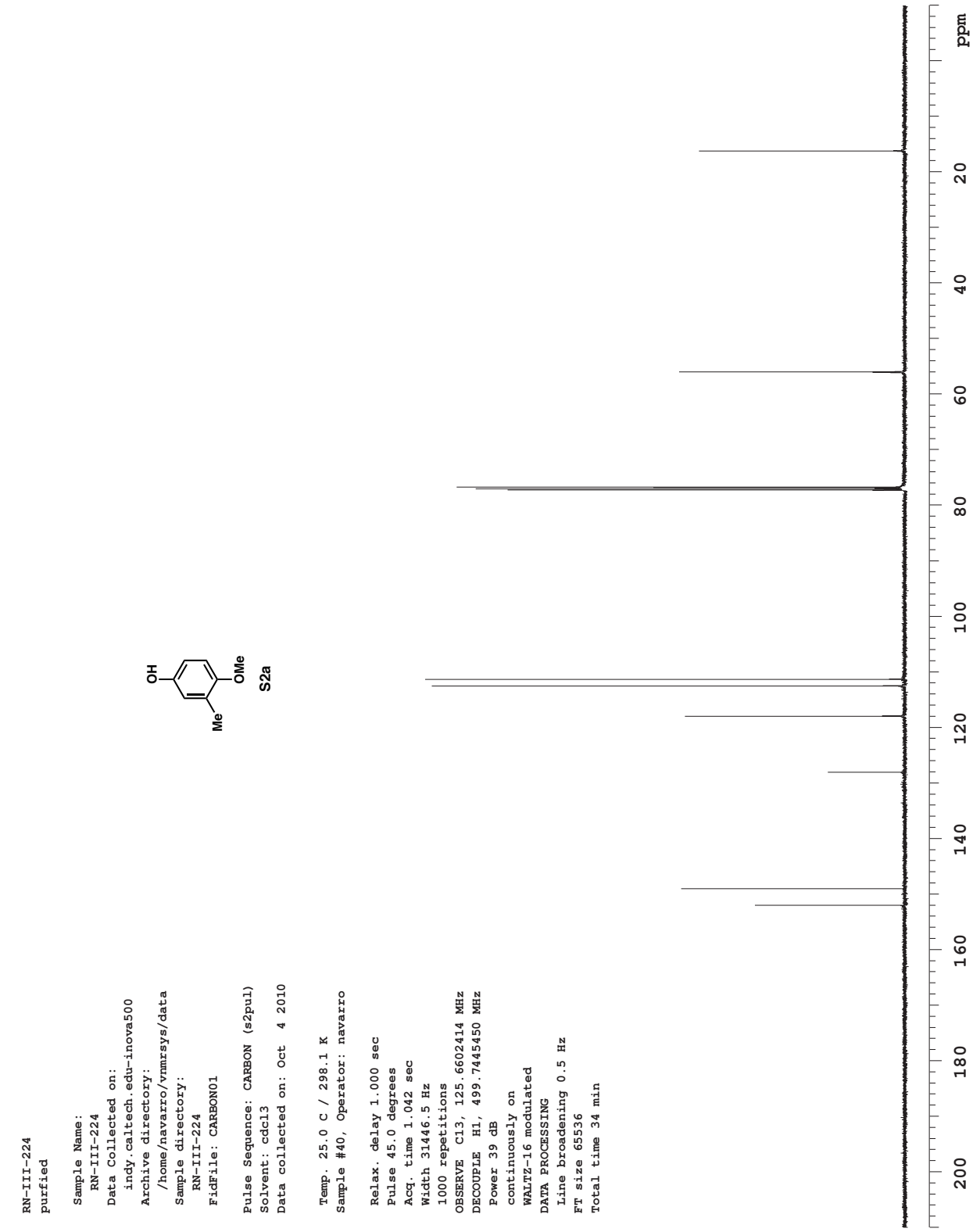
Sample directory:
RN-III-224
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 4 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 65536
Total time 1 min 12 sec
OH
OMe
Me
S2a
ppm
10
9
8
7
6
5
4
3
2
1
2.83
0.83
3.09
3.00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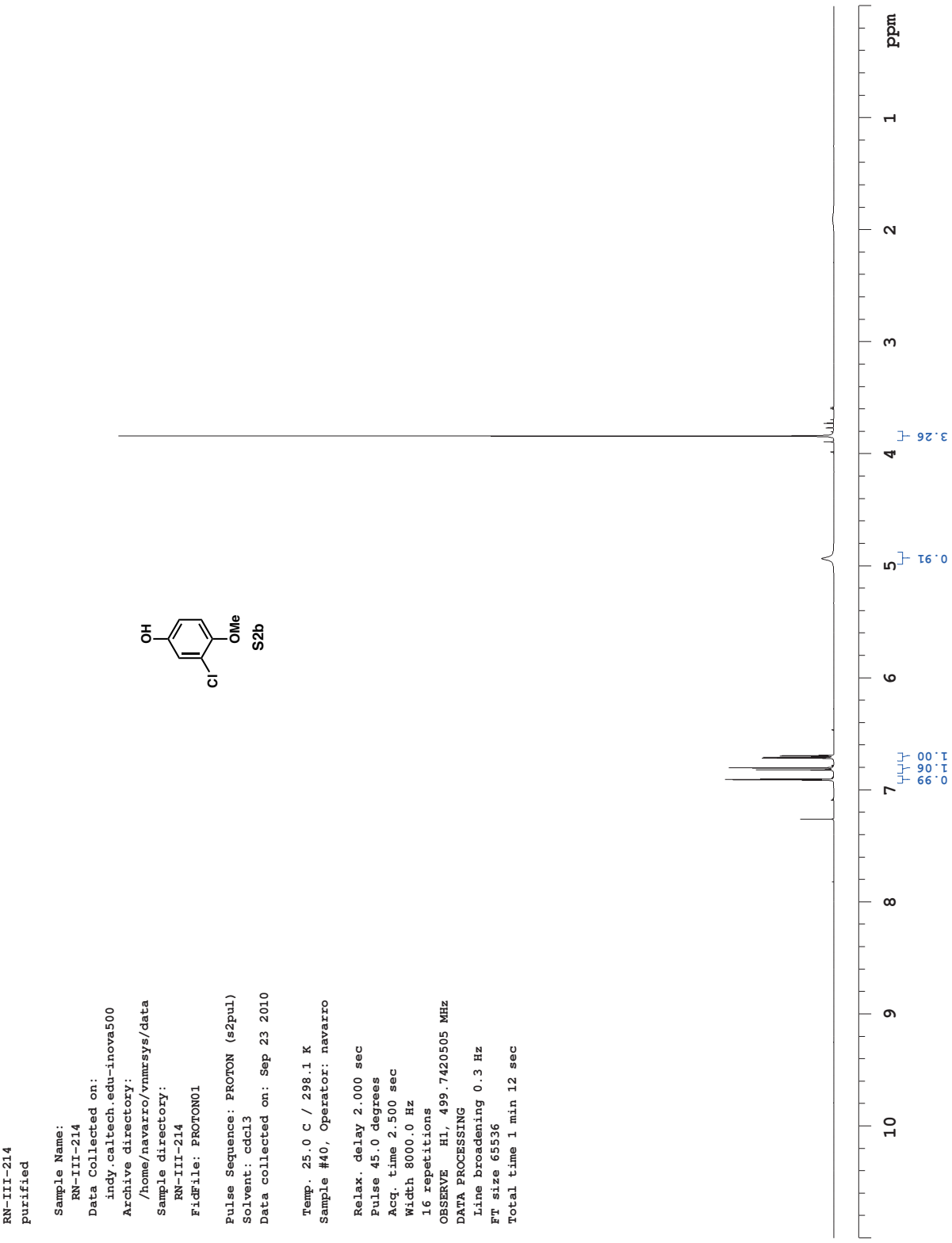
RN-III-224
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 4 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6602414 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
OH
OMe
Me
S2a
200
180
160
140
120
100
80
60
40
20
ppm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Sample directory:
RN-III-214
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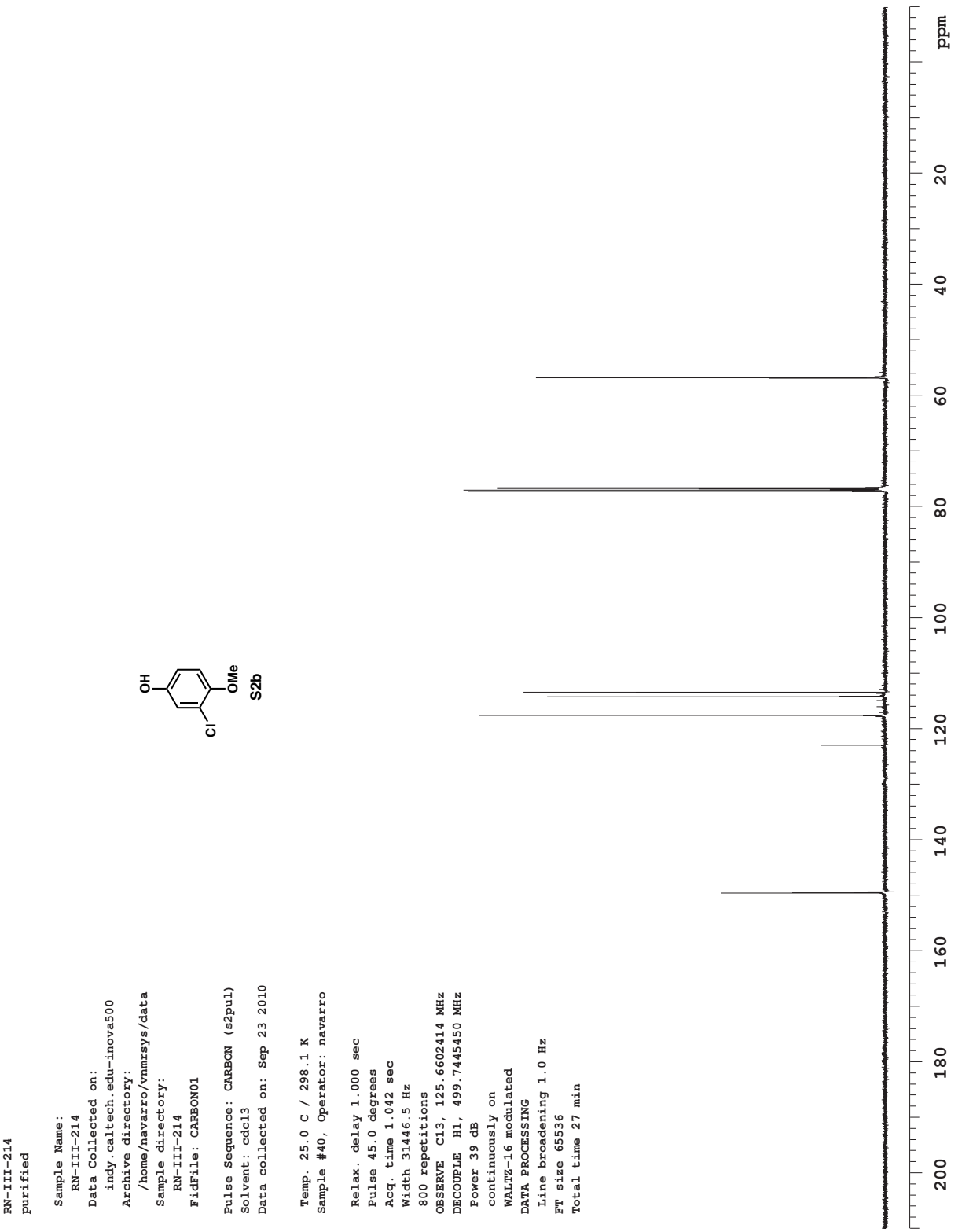
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 23 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
Line broadening 0.3 Hz
FT size 65536
Total time 1 min 12 sec
OH
OMe
Cl
S2b
3.26
0.91
0.99
1.06
1.00
ppm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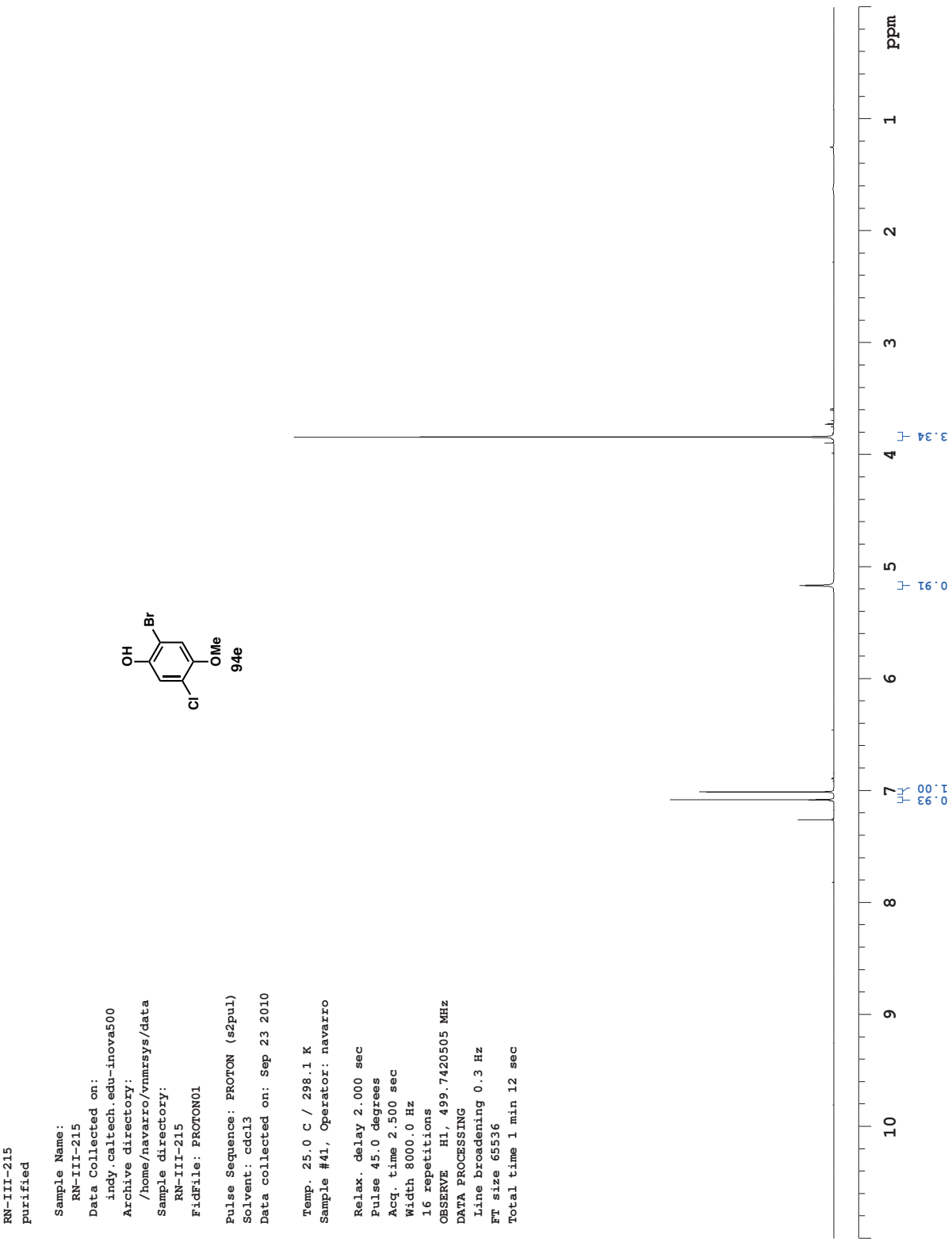
Sample directory:
RN-III-214
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 23 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
800 repetitions
OBSERVE C13, 125.6602414 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 27 min
OH
OMe
Cl
S2b
200
180
160
140
120
100
80
60
40
20
ppm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RN-III-215
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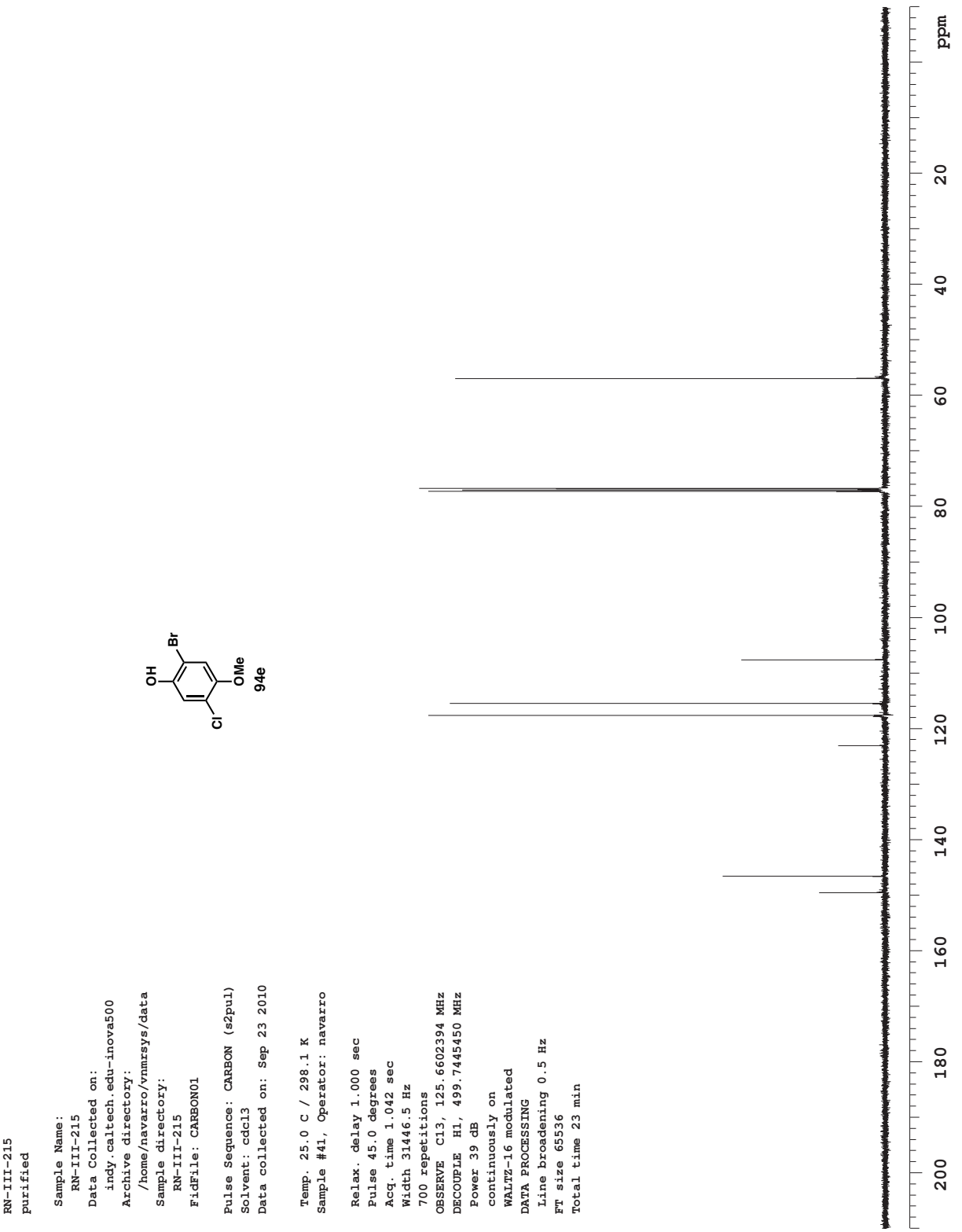
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 23 2010
Temp. 25.0 C / 298.1 K
Sample #41, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
Line broadening 0.3 Hz
FT size 65536
Total time 1 min 12 sec
OH
Br
OMe
Cl
94e
3.34
0.91
0.93
1.00
ppm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Sample directory:
RN-III-215
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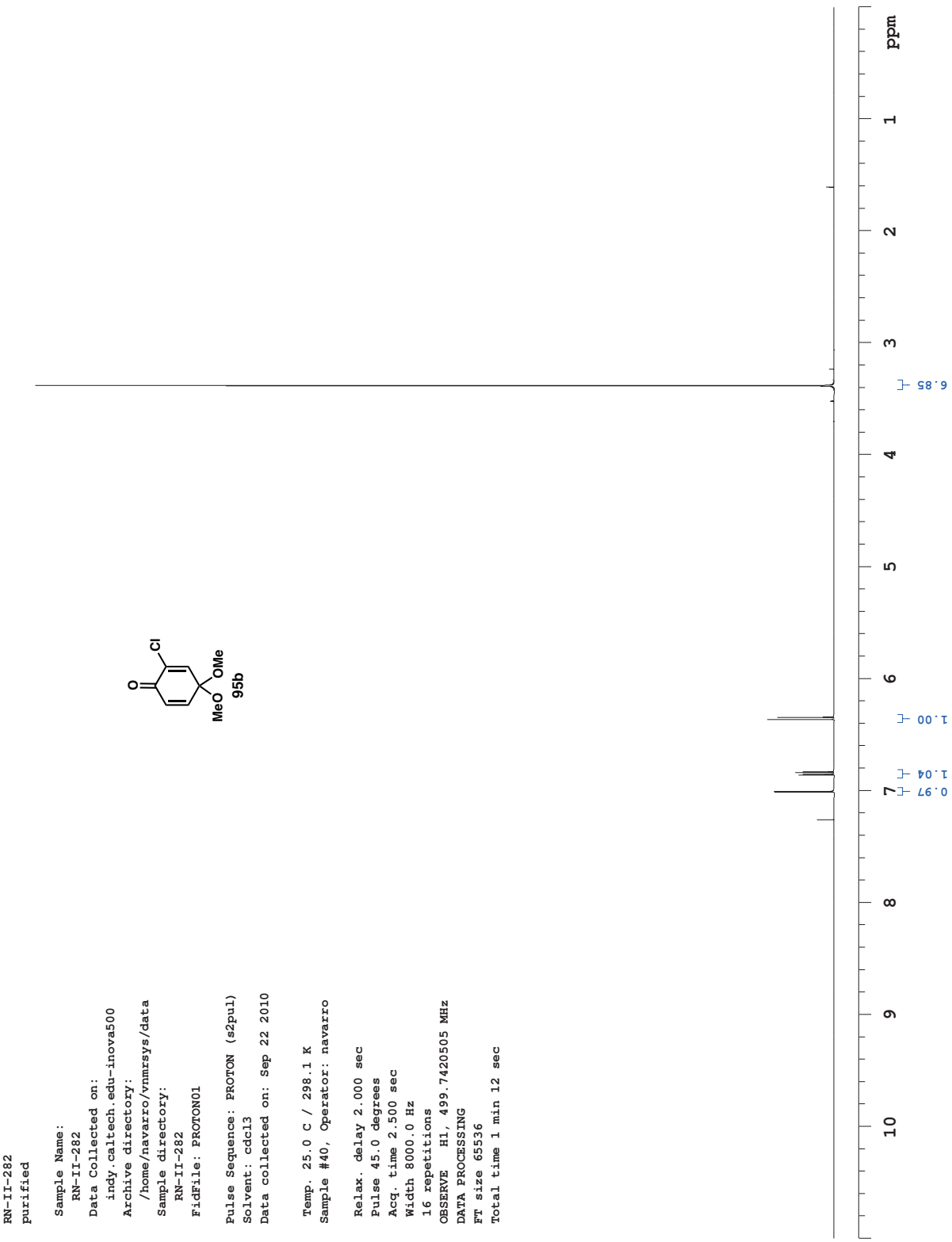
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 23 2010
Temp. 25.0 C / 298.1 K
Sample #41, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
700 repetitions
OBSERVE C13, 125.6602394 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 23 min
OH
Br
Cl
OMe
94e
200
180
160
140
120
100
80
60
40
20
ppm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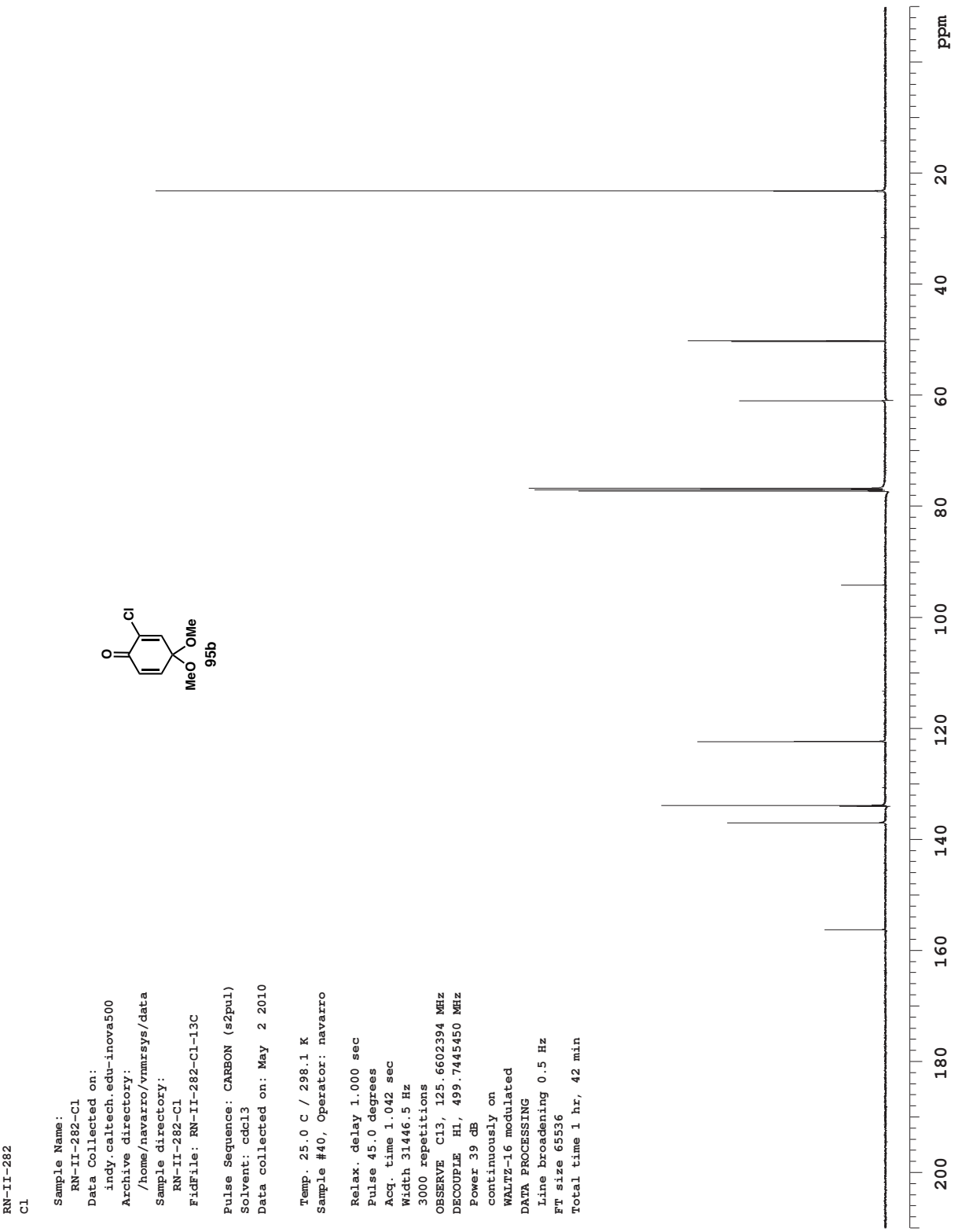
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-II-282
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 22 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 65536
Total time 1 min 12 sec
Cl
O
MeO
OMe
95b
ppm
10
9
8
7
6
5
4
3
2
1
6.85
1.00
1.04
0.97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Cl
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Archive directory:
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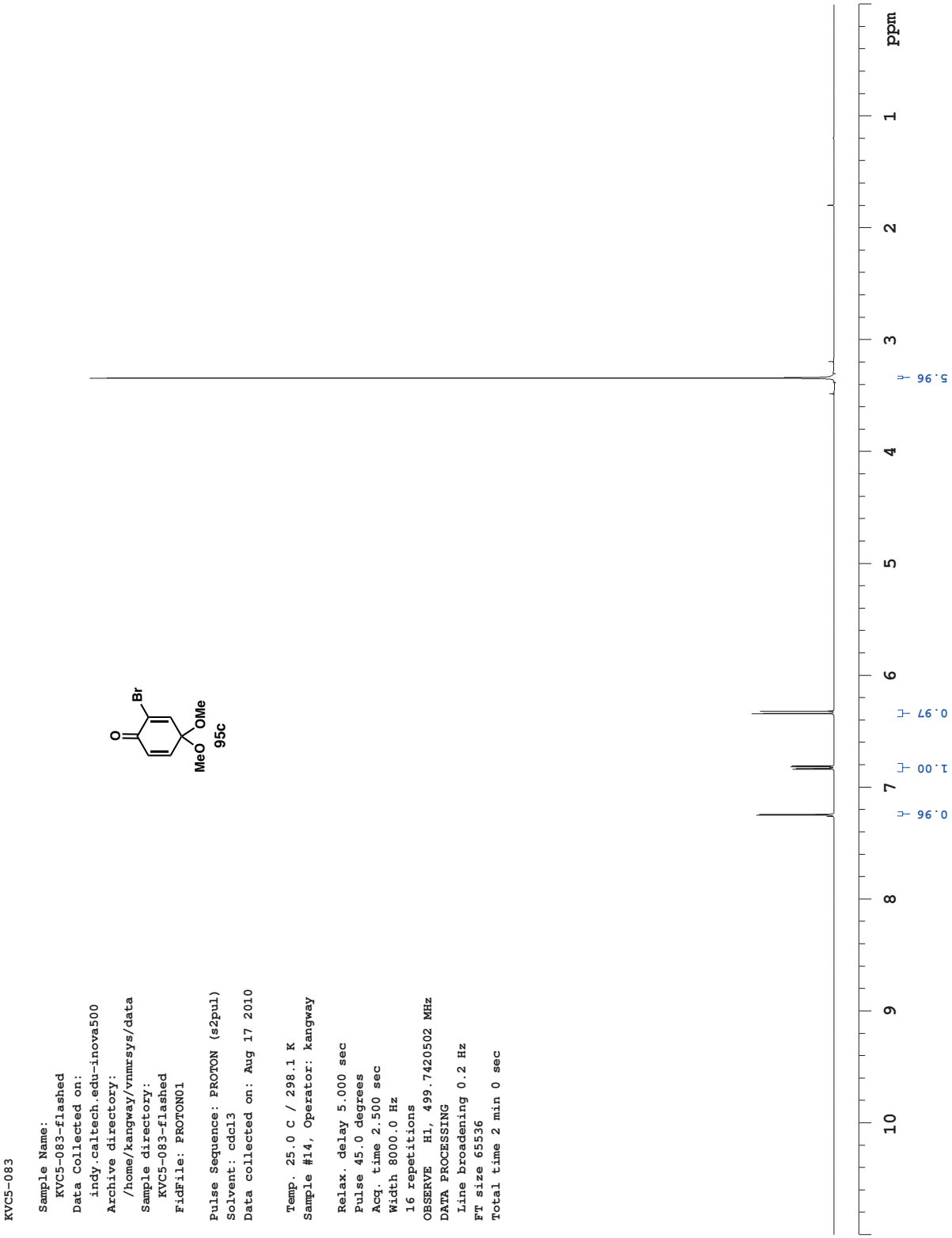
Sample directory:
RN-II-282-Cl
FidFile: RN-II-282-Cl-13C
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 2 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
3000 repetitions
OBSERVE C13, 125.6602394 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 42 min
Cl
O
MeO
OMe
95b
200
180
160
140
120
100
80
60
40
20
ppm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Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 17 2010
Temp. 25.0 C / 298.1 K
Sample #14, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420502 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 2 min 0 sec
Br
O
MeO
OMe
95c
10
9
8
7
6
5
4
3
2
1
ppm
0.96
1.00
0.97
5.96

KVC5-083-flashed

Sample Name:
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Data Collected on:
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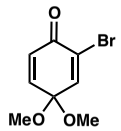
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC5-083-flashed
FidFile: CARBON01

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 17 2010

Temp. 25.0 C / 298.1 K
Sample #14, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
300 repetitions
OBSERVE C13, 125.6602538 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 10 min



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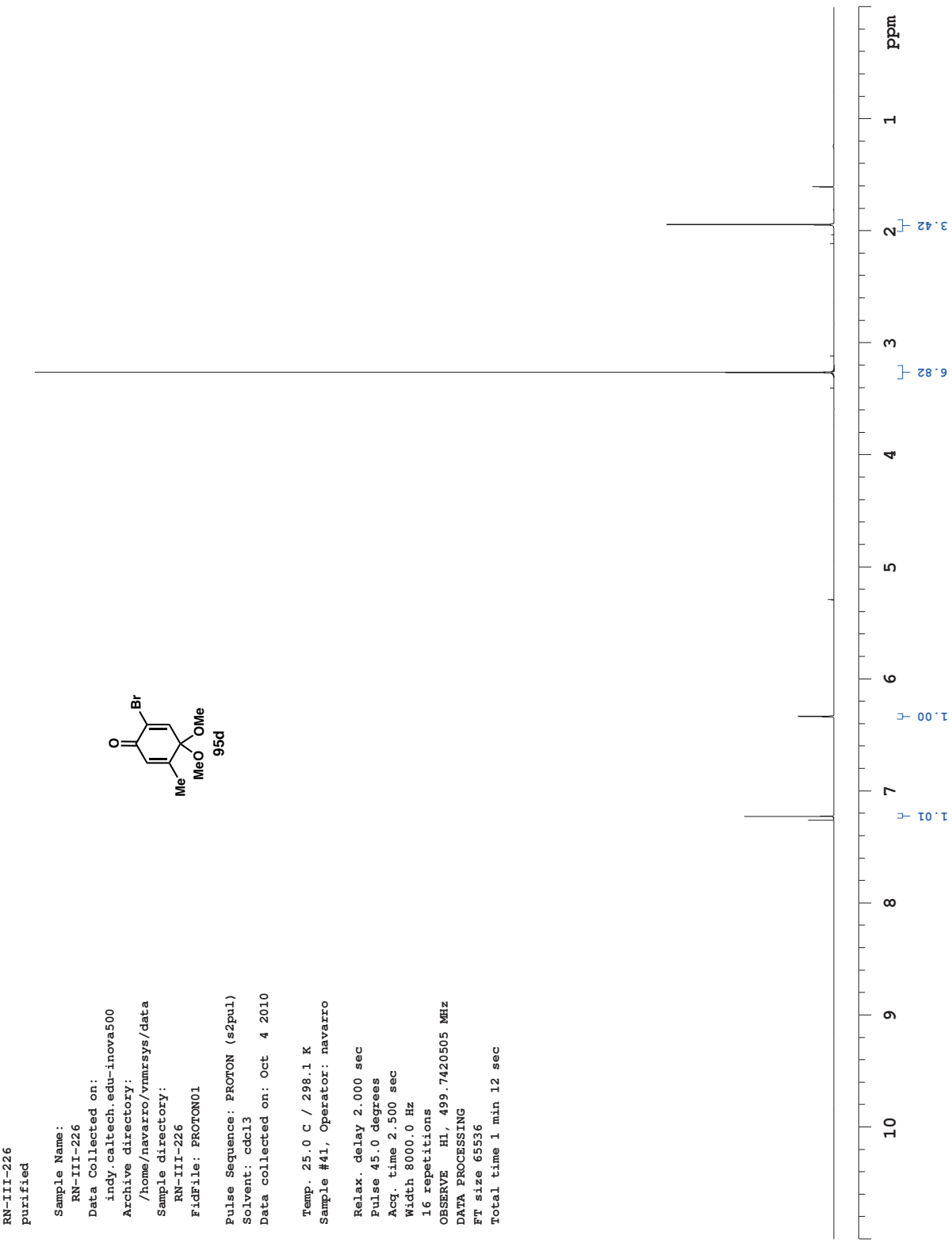
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Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 4 2010
Temp. 25.0 C / 298.1 K
Sample #41, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 65536
Total time 1 min 12 sec
O
Br
Me
MeO
OMe
95d
ppm
10
9
8
7
6
5
4
3
2
1
1.01
1.00
6.82
3.42

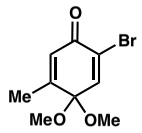
RN-III-226
purified

Sample Name:
RN-III-226
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-226
FidFile: CARBON01

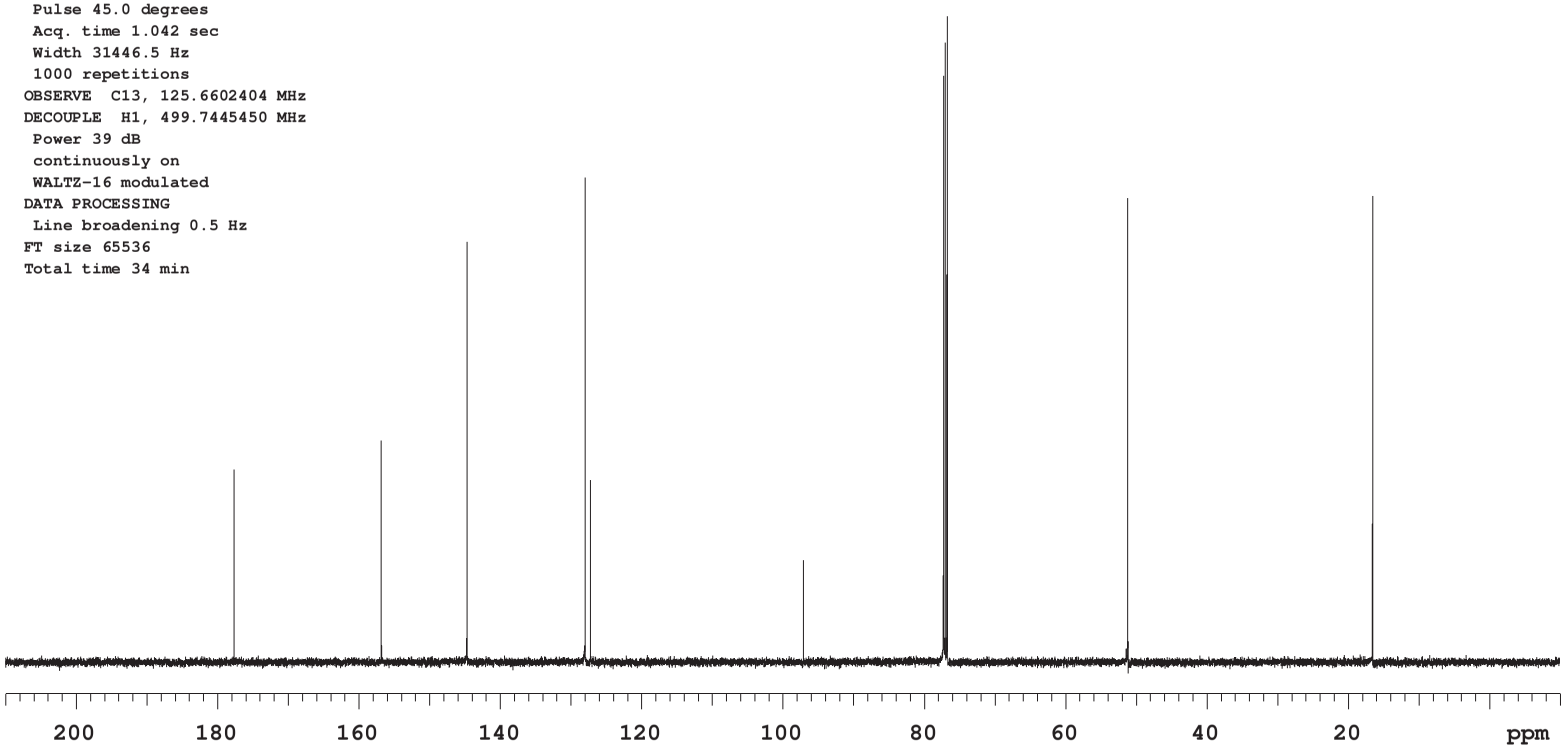
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 4 2010

Temp. 25.0 C / 298.1 K
Sample #41, Operator: navarro

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6602404 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min



95d



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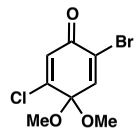
RN-III-218
FidFile: PROTON01

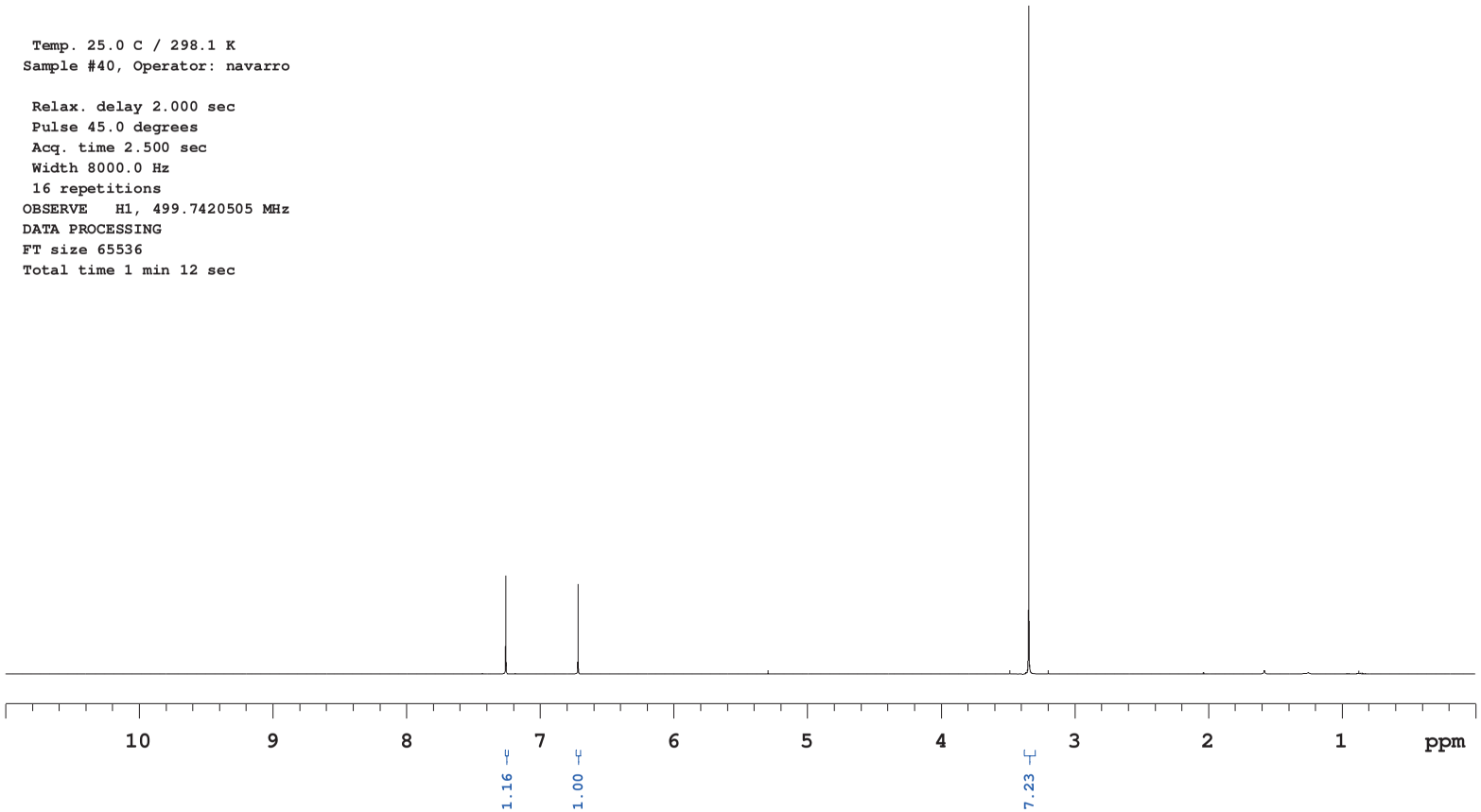
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 6 2010

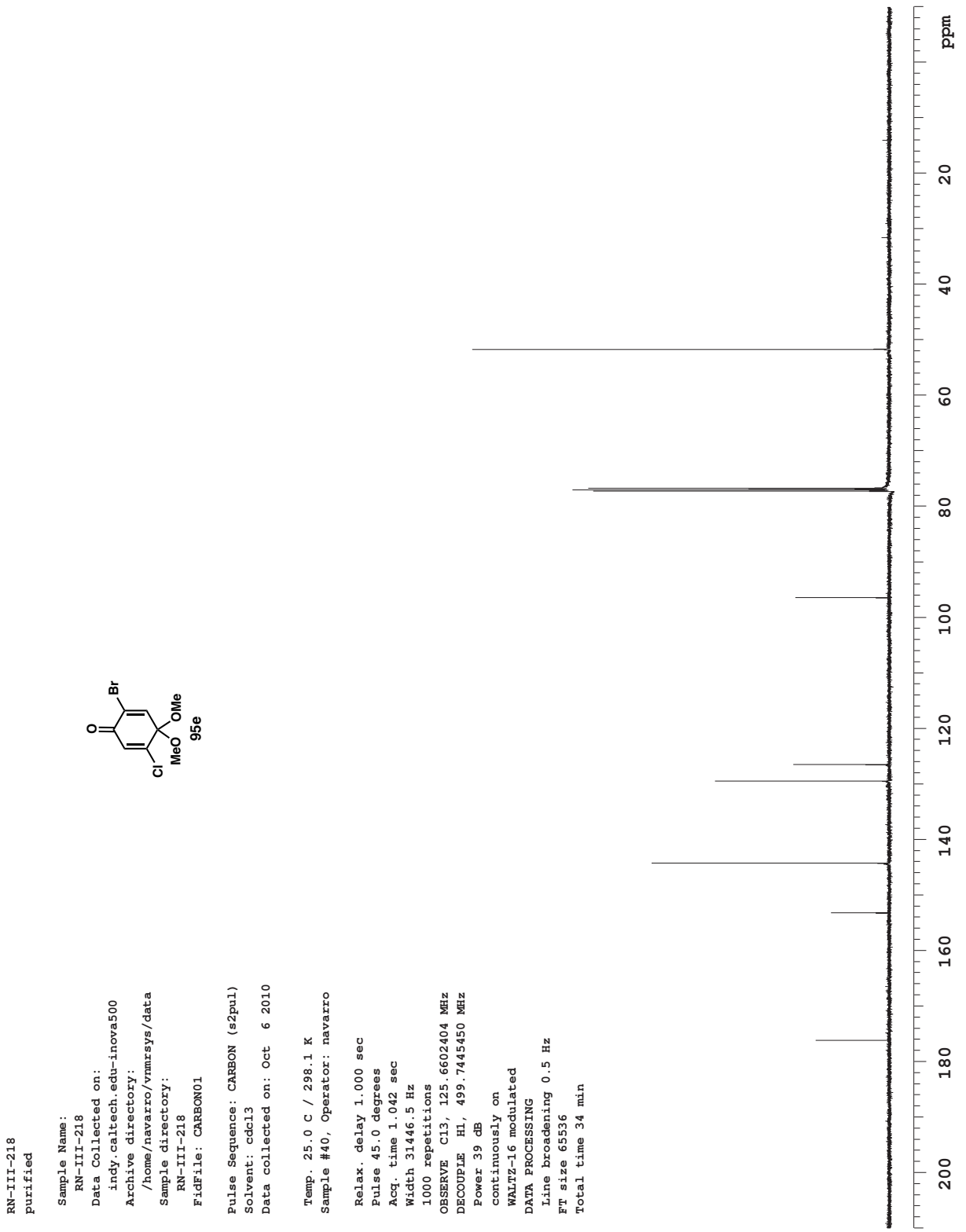
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro

Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 65536
Total time 1 min 12 sec



95e

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Data Collected on:
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Archive directory:
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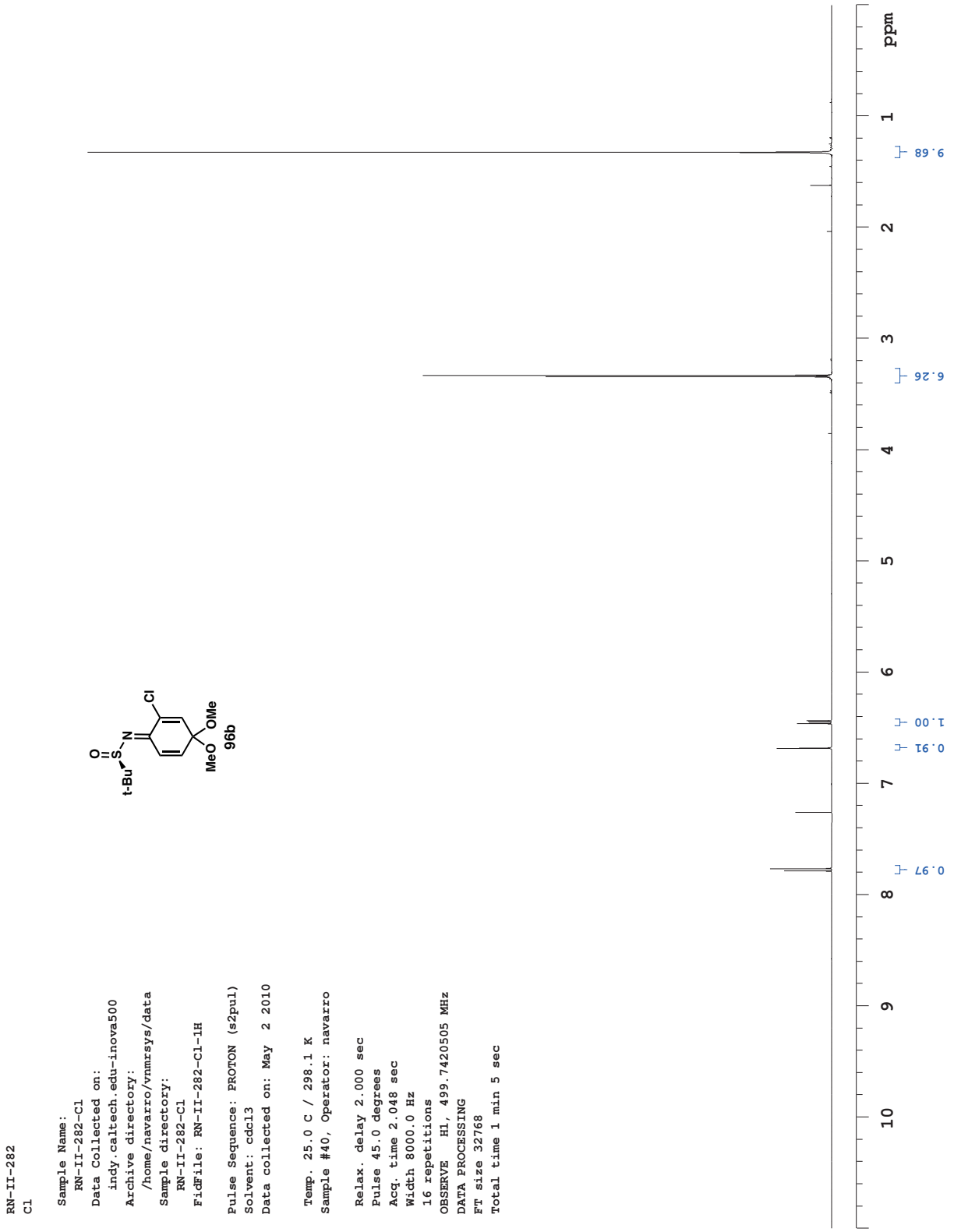
Sample directory:
RN-III-218
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 6 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6602404 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
O
Br
Cl
MeO
OMe
95e
200
180
160
140
120
100
80
60
40
20
ppm


RN-II-282
Cl
Sample Name:
RN-II-282-Cl
Data Collected on:
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Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-II-282-Cl
FidFile: RN-II-282-Cl-1H
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 2 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 32768
Total time 1 min 5 sec
t-Bu
O
S
N
Cl
MeO
OMe
96b
ppm
10
9
8
7
6
5
4
3
2
1
0.97
0.91
1.00
6.26
9.68

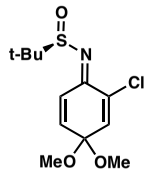
RN-II-282
Cl

Sample Name:
RN-II-282-Cl
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-II-282-Cl
FidFile: RN-II-282-Cl-13C

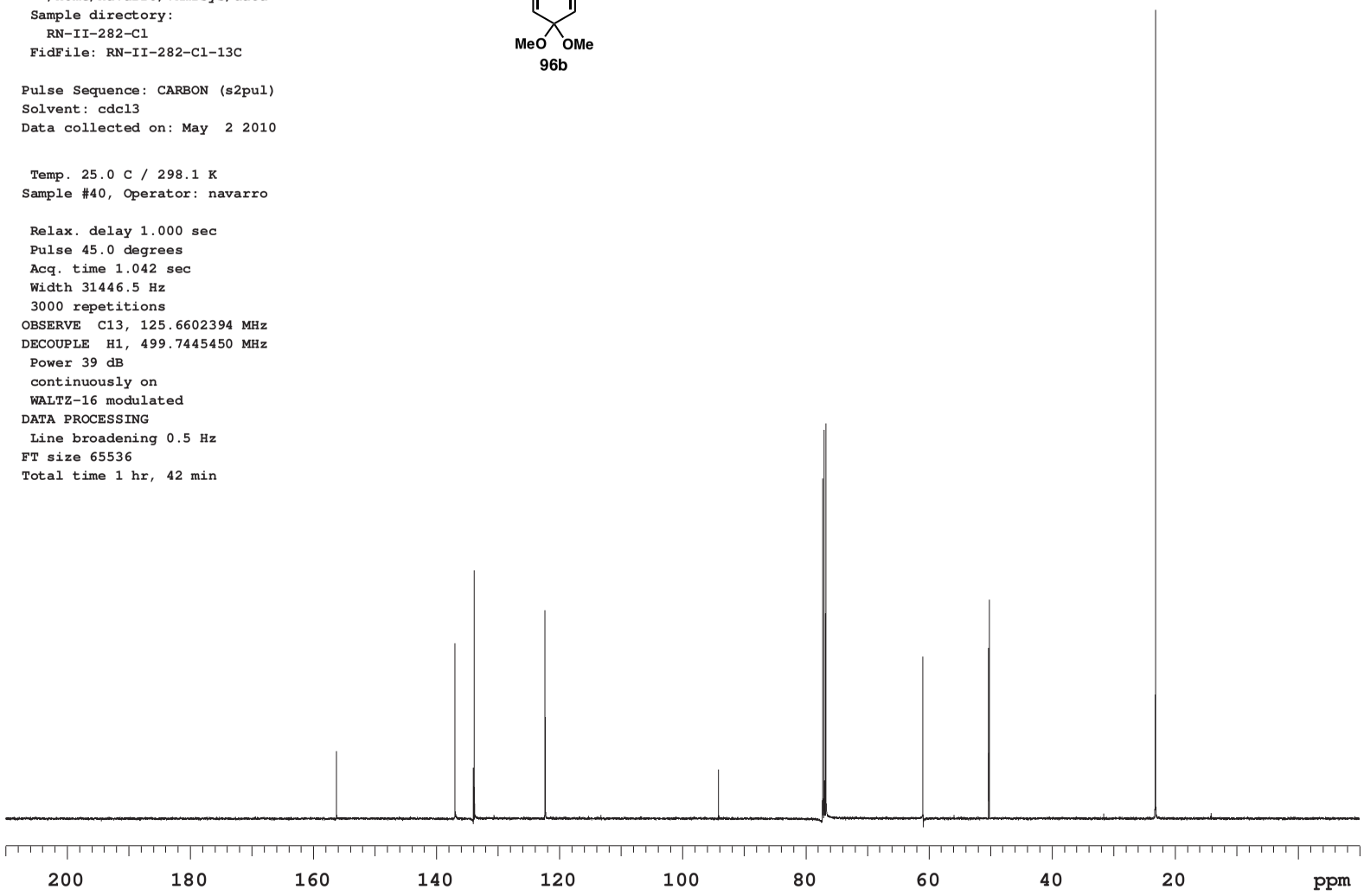
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 2 2010

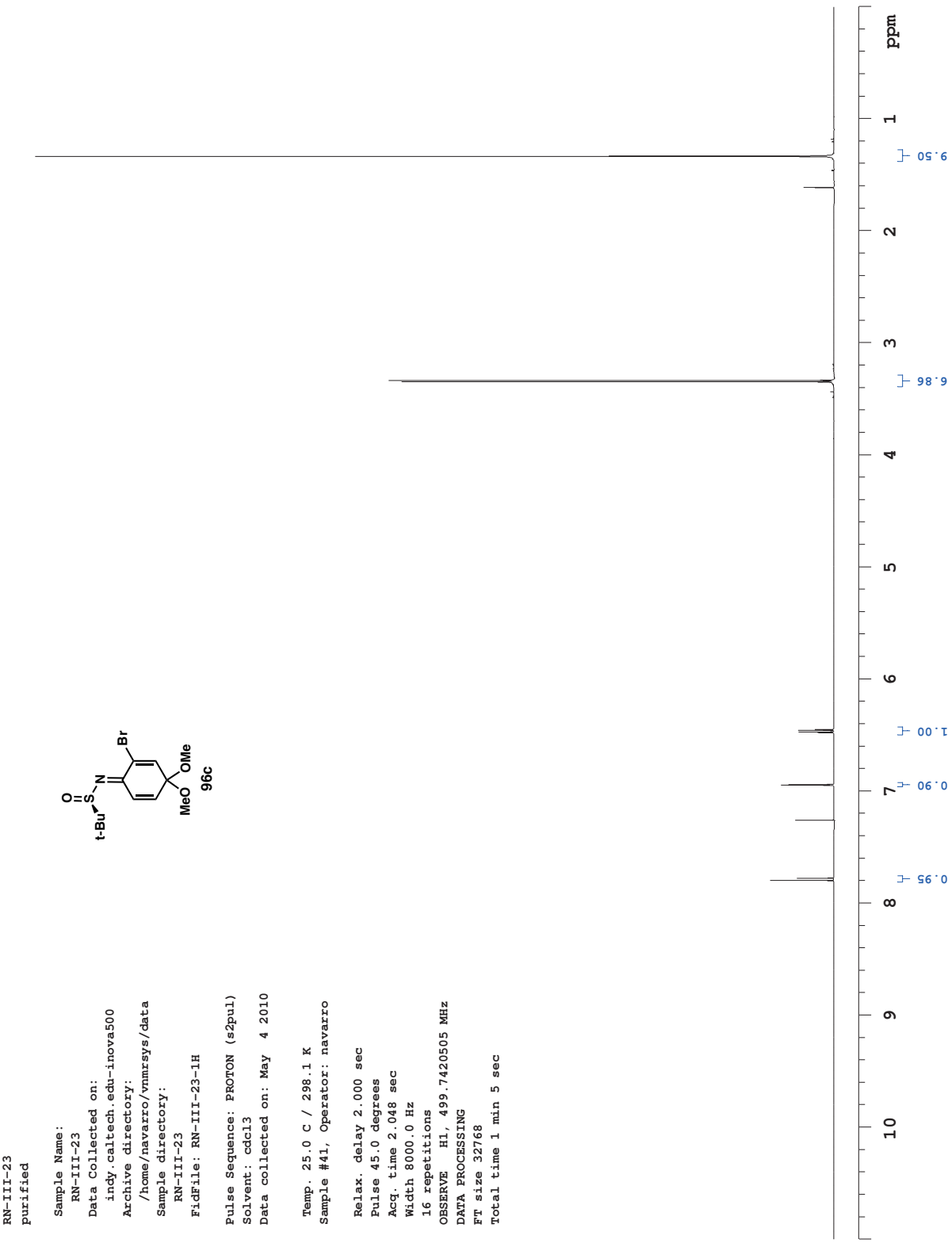
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro

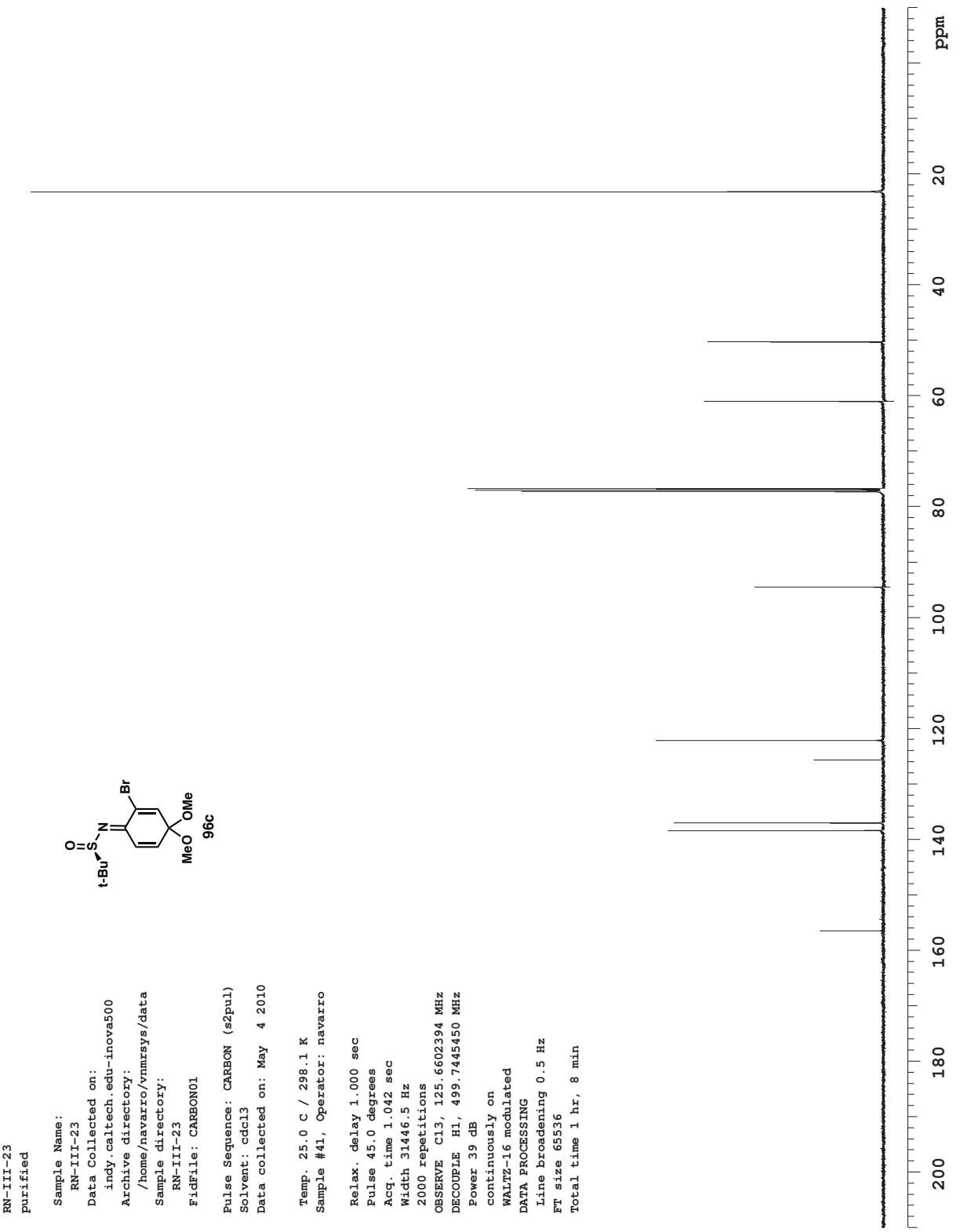
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
3000 repetitions
OBSERVE C13, 125.6602394 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 42 min

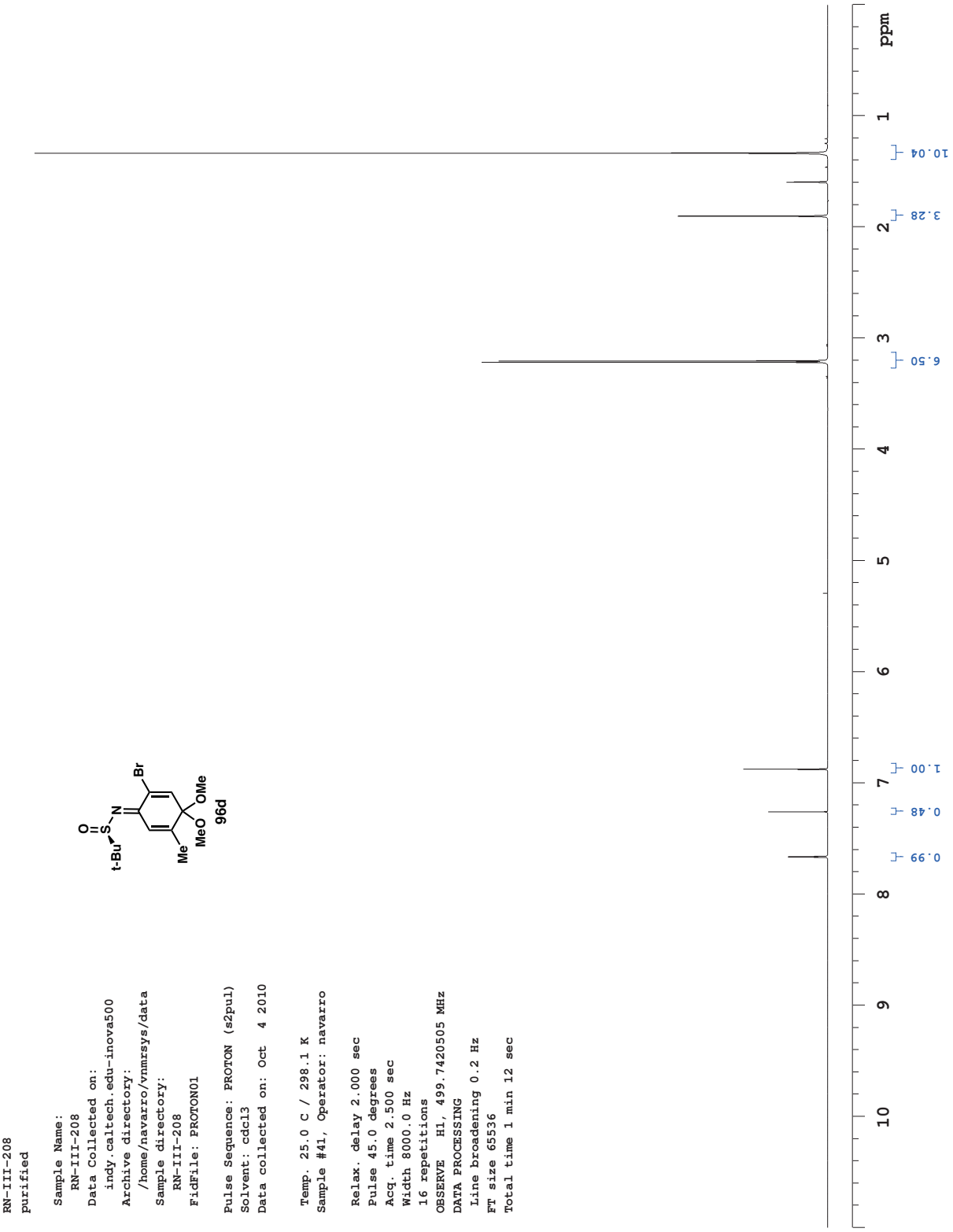


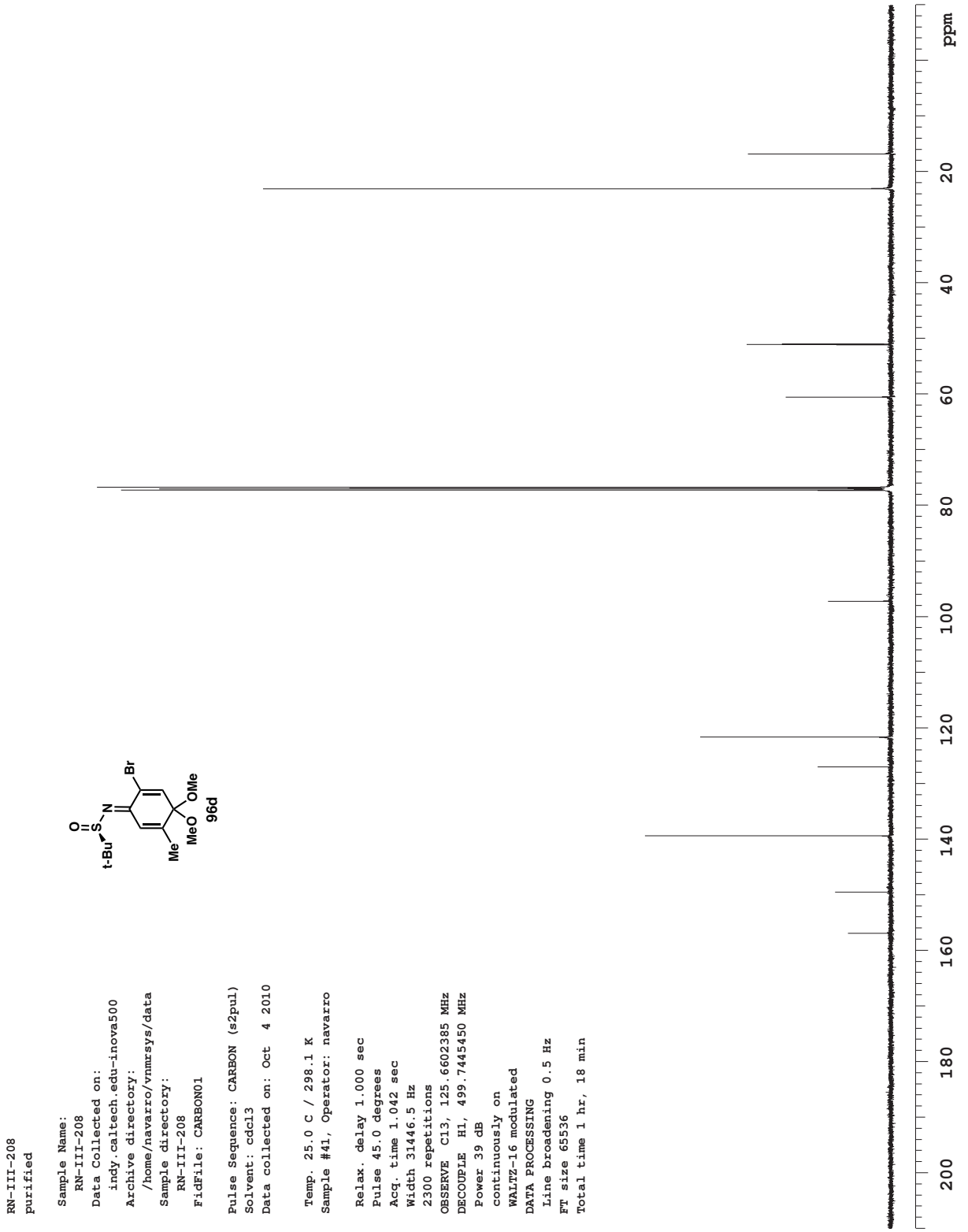
96b

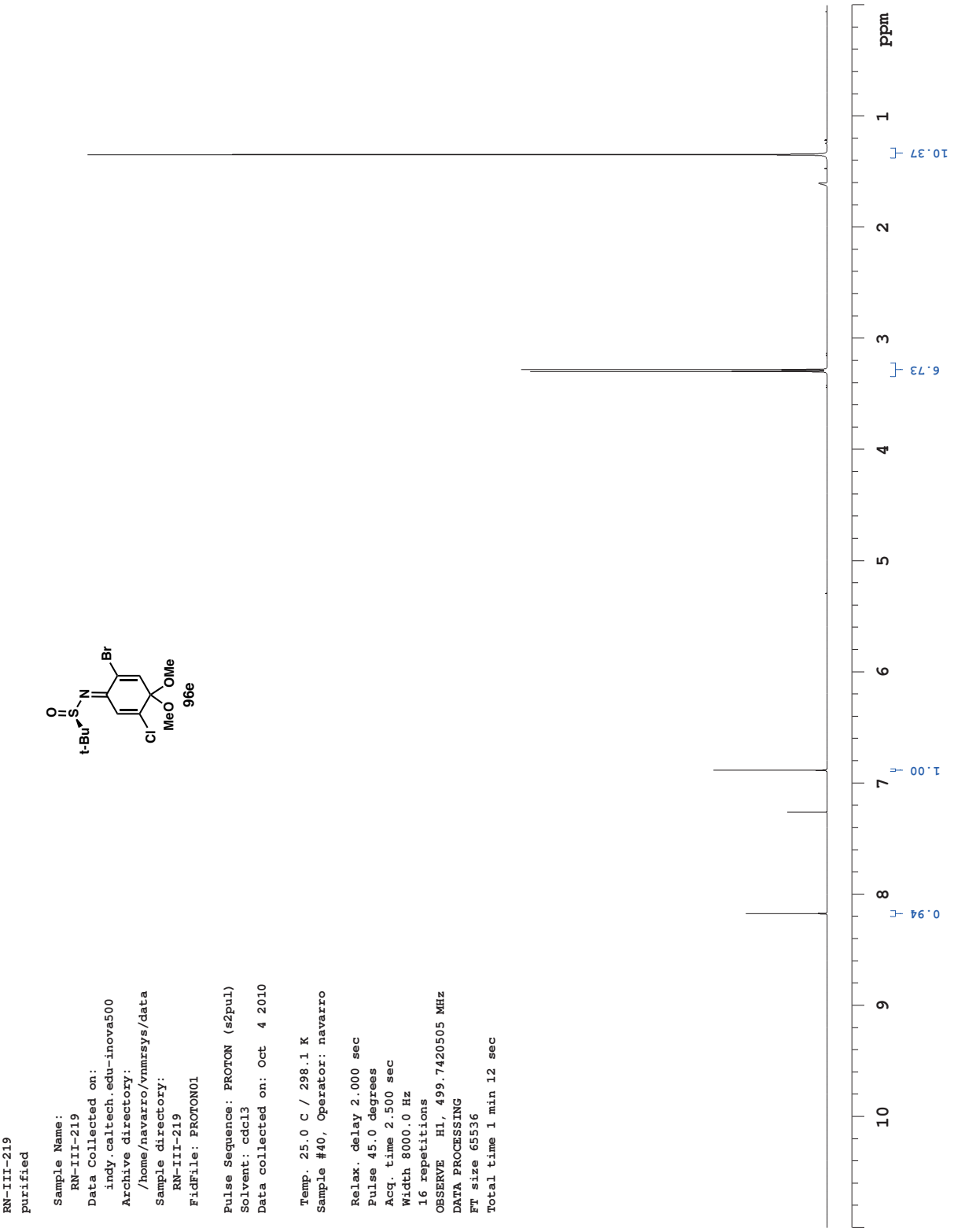



RN-III-23
purified
Sample Name:
RN-III-23
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-23
FidFile: RN-III-23-1H
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 4 2010
Temp. 25.0 C / 298.1 K
Sample #41, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 32768
Total time 1 min 5 sec
t-Bu
O
S
N
Br
OMe
MeO
96c
ppm
9.50
6.86
1.00
0.90
0.95


RN-III-23
purified
Sample Name:
RN-III-23
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-23
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 4 2010
Temp. 25.0 C / 298.1 K
Sample #41, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2000 repetitions
OBSERVE C13, 125.6602394 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 8 min
t-Bu
Br
MeO
OMe
96c
200
180
160
140
120
100
80
60
40
20
ppm


RN-III-208
purified
Sample Name:
RN-III-208
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-208
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 4 2010
Temp. 25.0 C / 298.1 K
Sample #41, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 1 min 12 sec
O
S
N
t-Bu
Br
Me
MeO
OMe
96d
ppm
10
9
8
7
6
5
4
3
2
1
0.99
0.48
1.00
6.50
3.28
10.04


RN-III-208
purified
Sample Name:
RN-III-208
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-208
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 4 2010
Temp. 25.0 C / 298.1 K
Sample #41, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2300 repetitions
OBSERVE C13, 125.6602385 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 18 min
t-Bu
Me
MeO
OMe
Br
96d
200
180
160
140
120
100
80
60
40
20
ppm


RN-III-219
purified
Sample Name:
RN-III-219
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-219
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 4 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 65536
Total time 1 min 12 sec
t-Bu
O
S
N
Br
Cl
MeO
OMe
96e
ppm
10.37
6.73
1.00
0.94

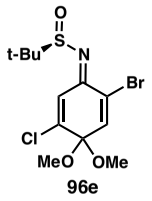
RN-III-219
purified

Sample Name:
RN-III-219
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-219
FidFile: CARBON01

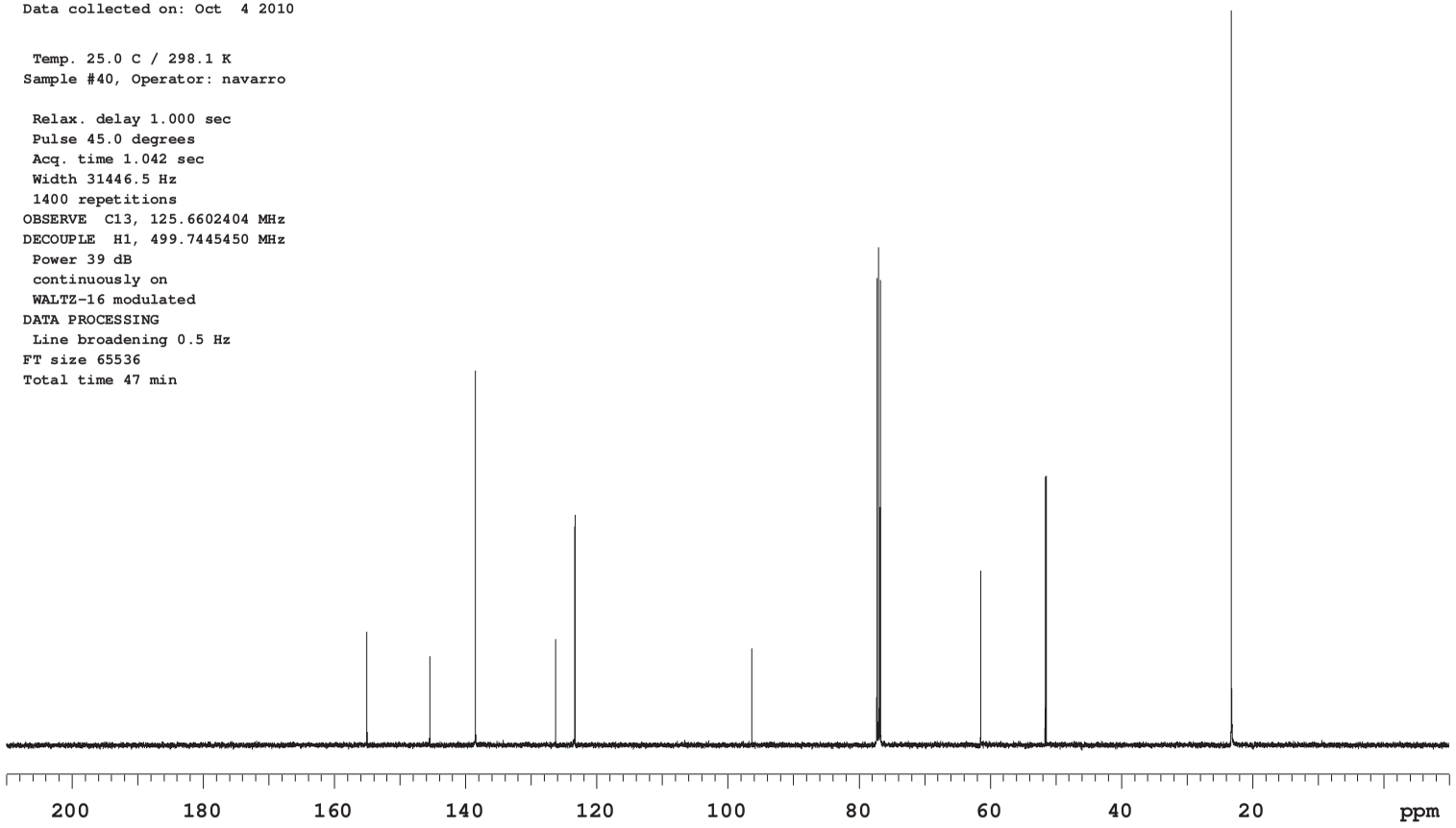
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 4 2010

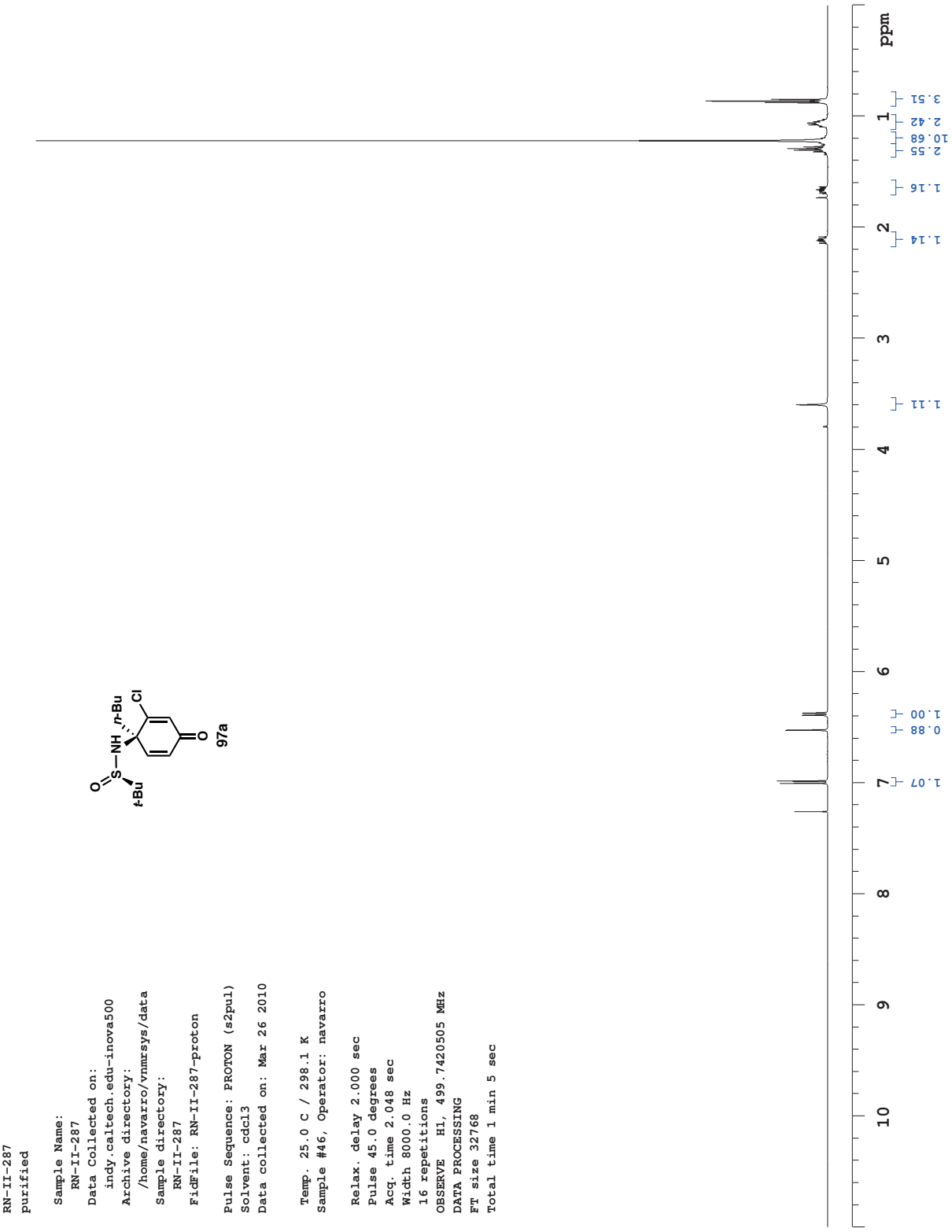
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro

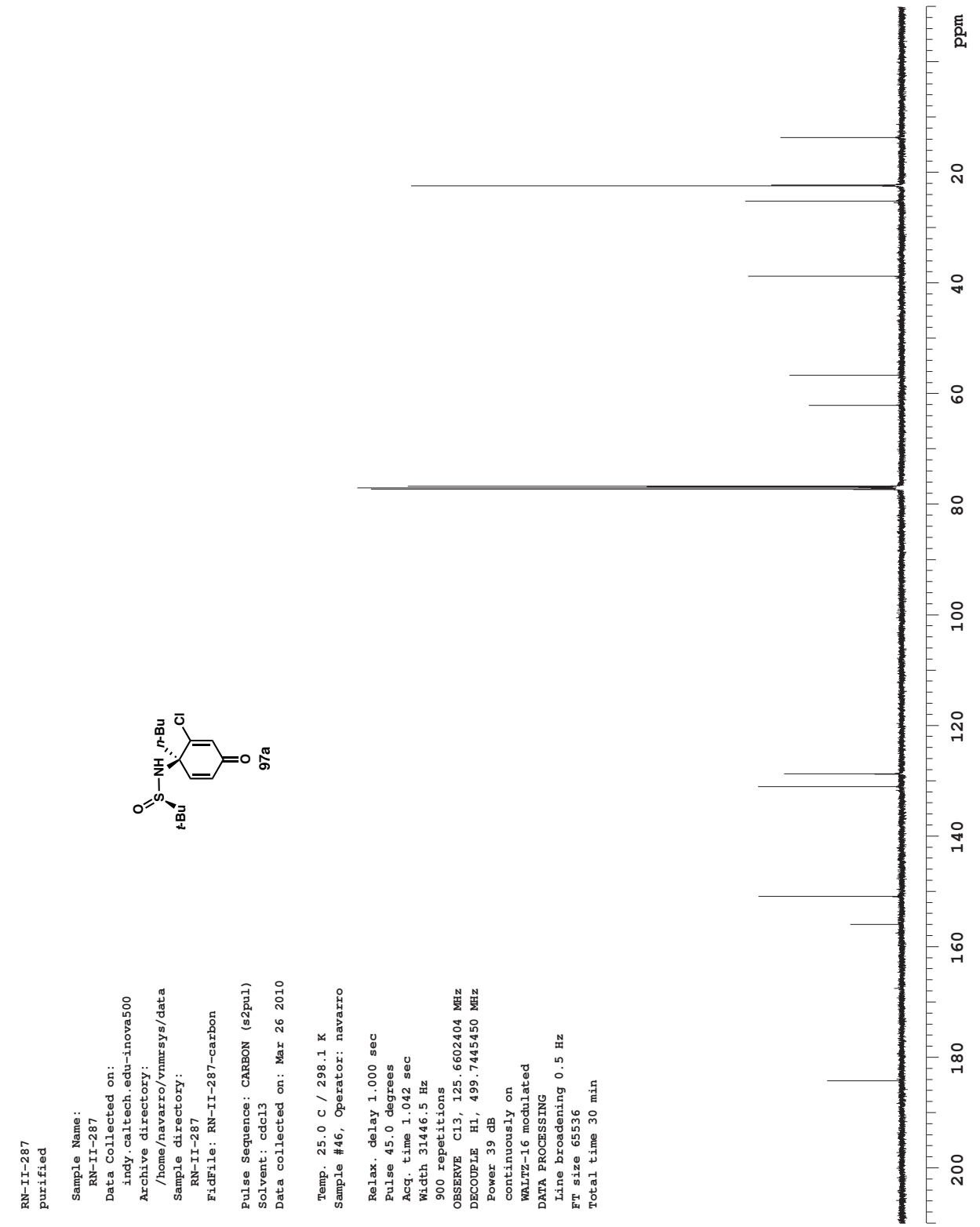
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1400 repetitions
OBSERVE C13, 125.6602404 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 47 min

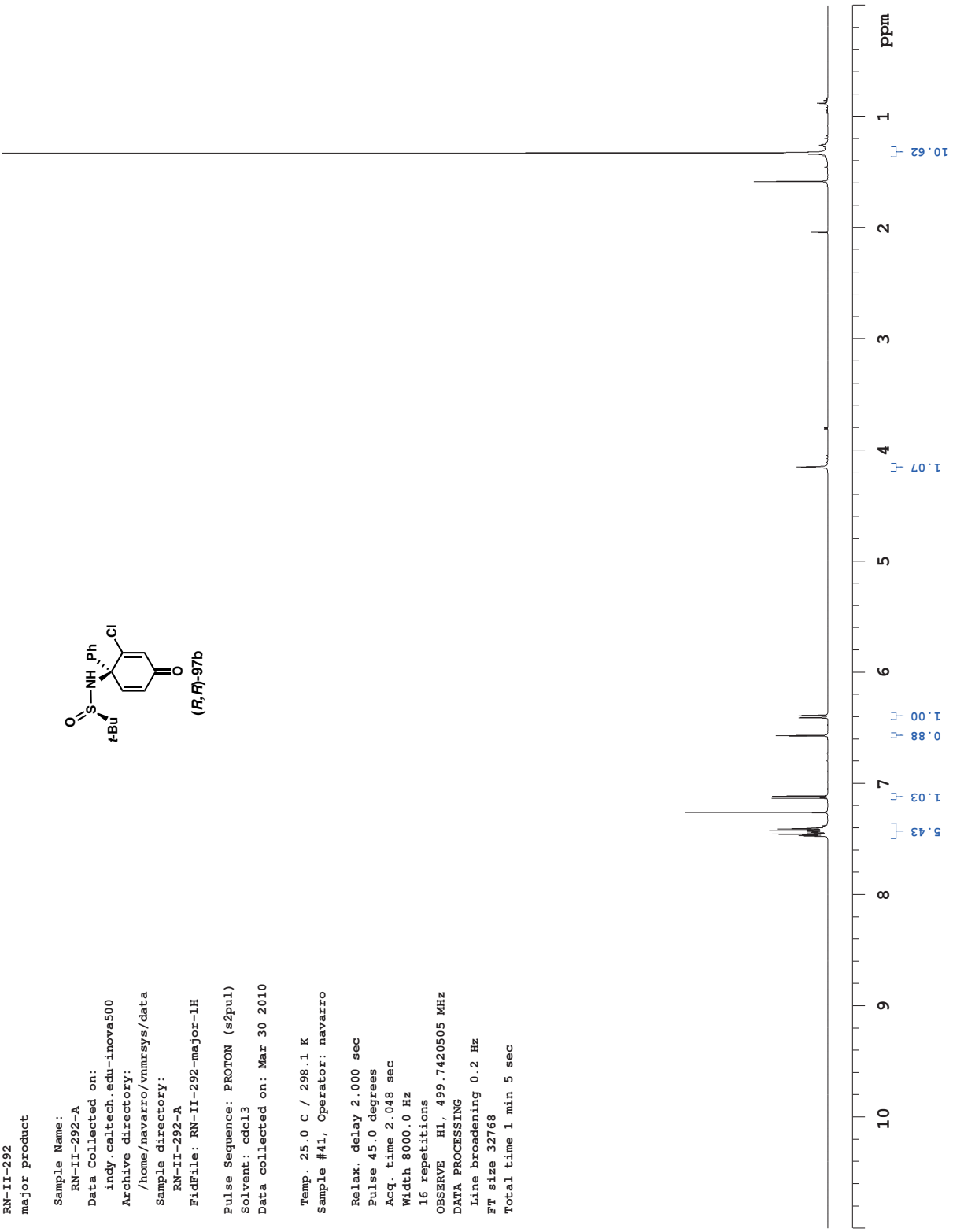


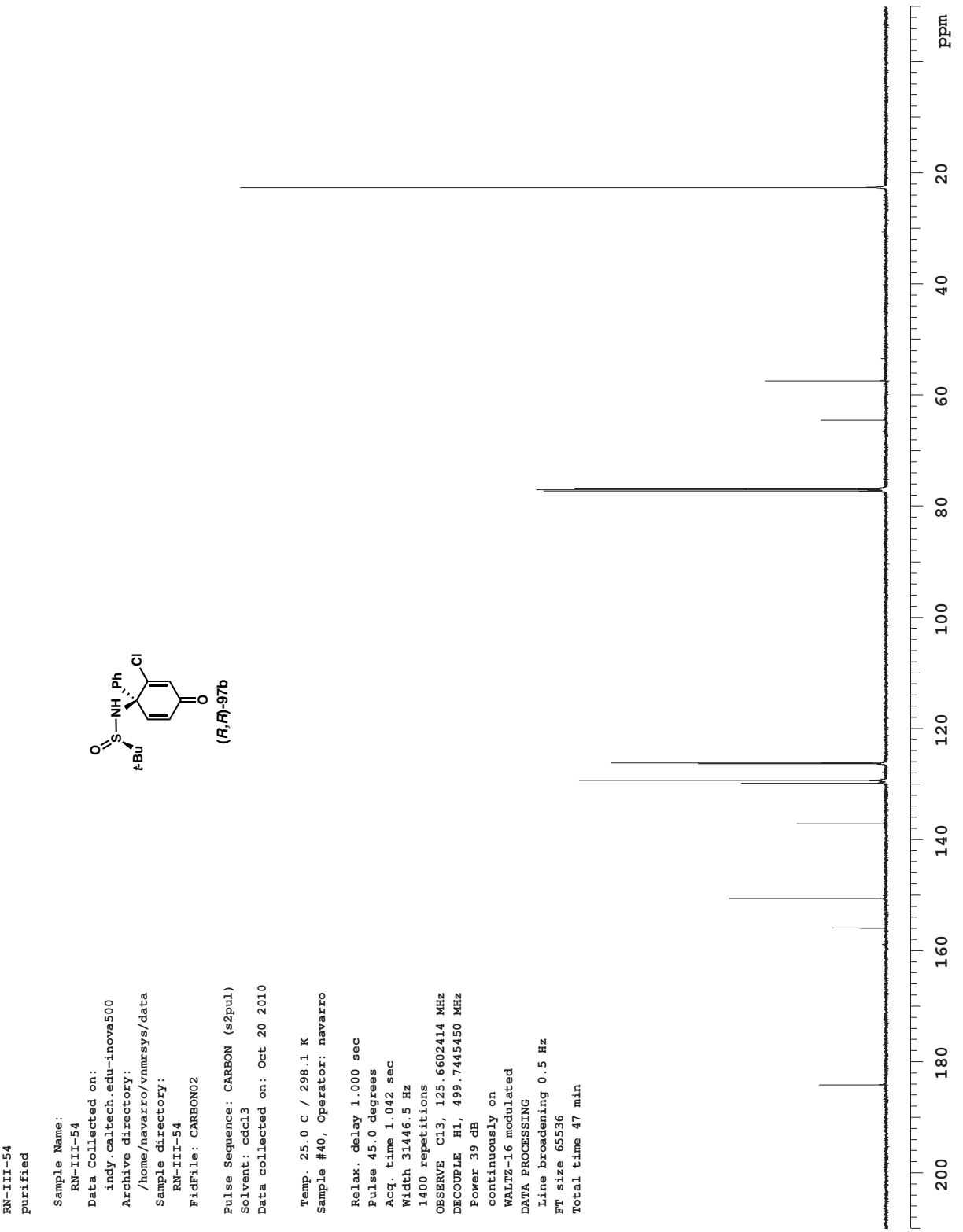
96e

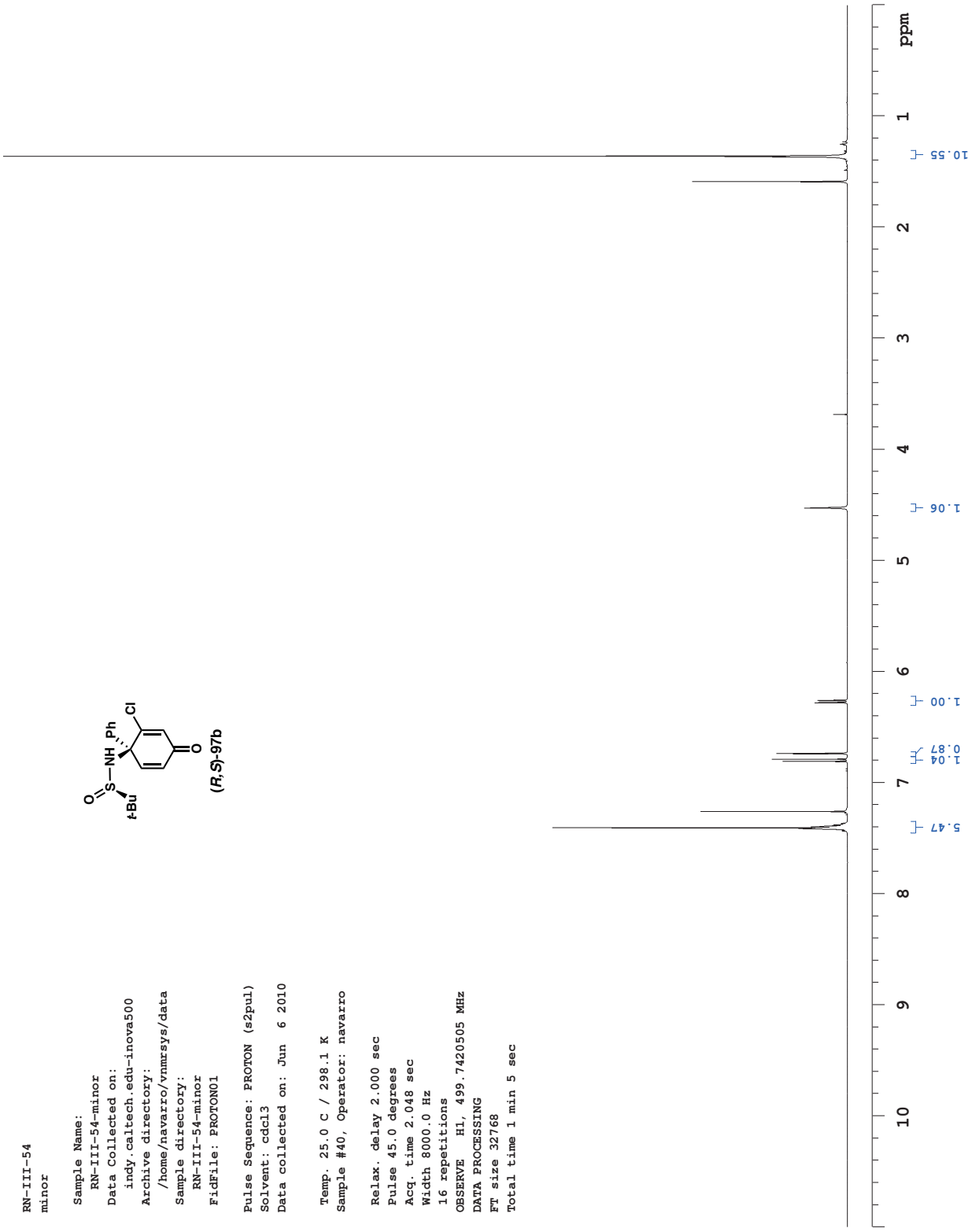


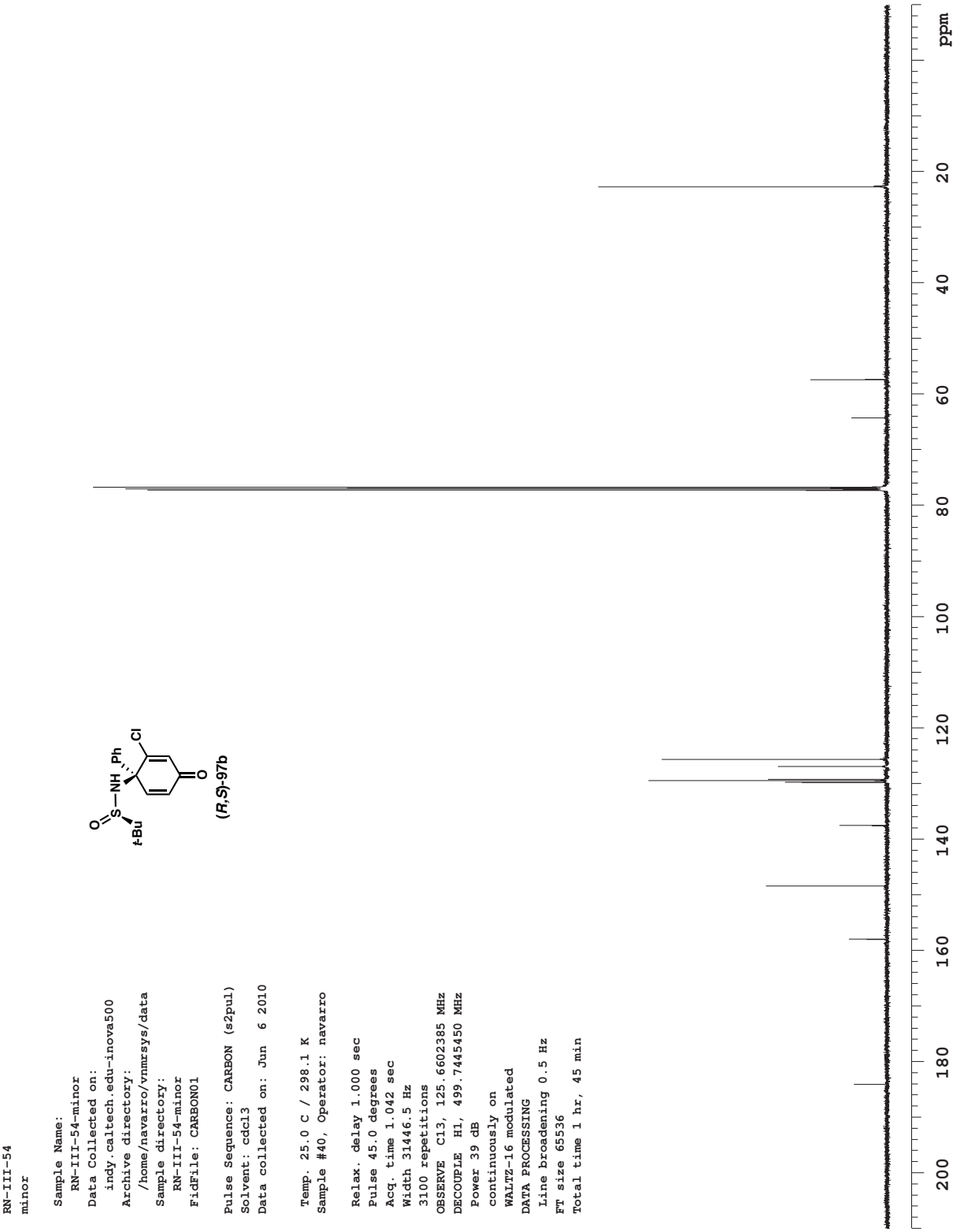

RN-II-287
purified
Sample Name:
RN-II-287
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-II-287
FidFile: RN-II-287-proton
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 26 2010
Temp. 25.0 C / 298.1 K
Sample #46, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 32768
Total time 1 min 5 sec
97a
ppm
3.51
2.42
10.68
2.55
1.16
1.14
1.11
1.00
0.88
1.07

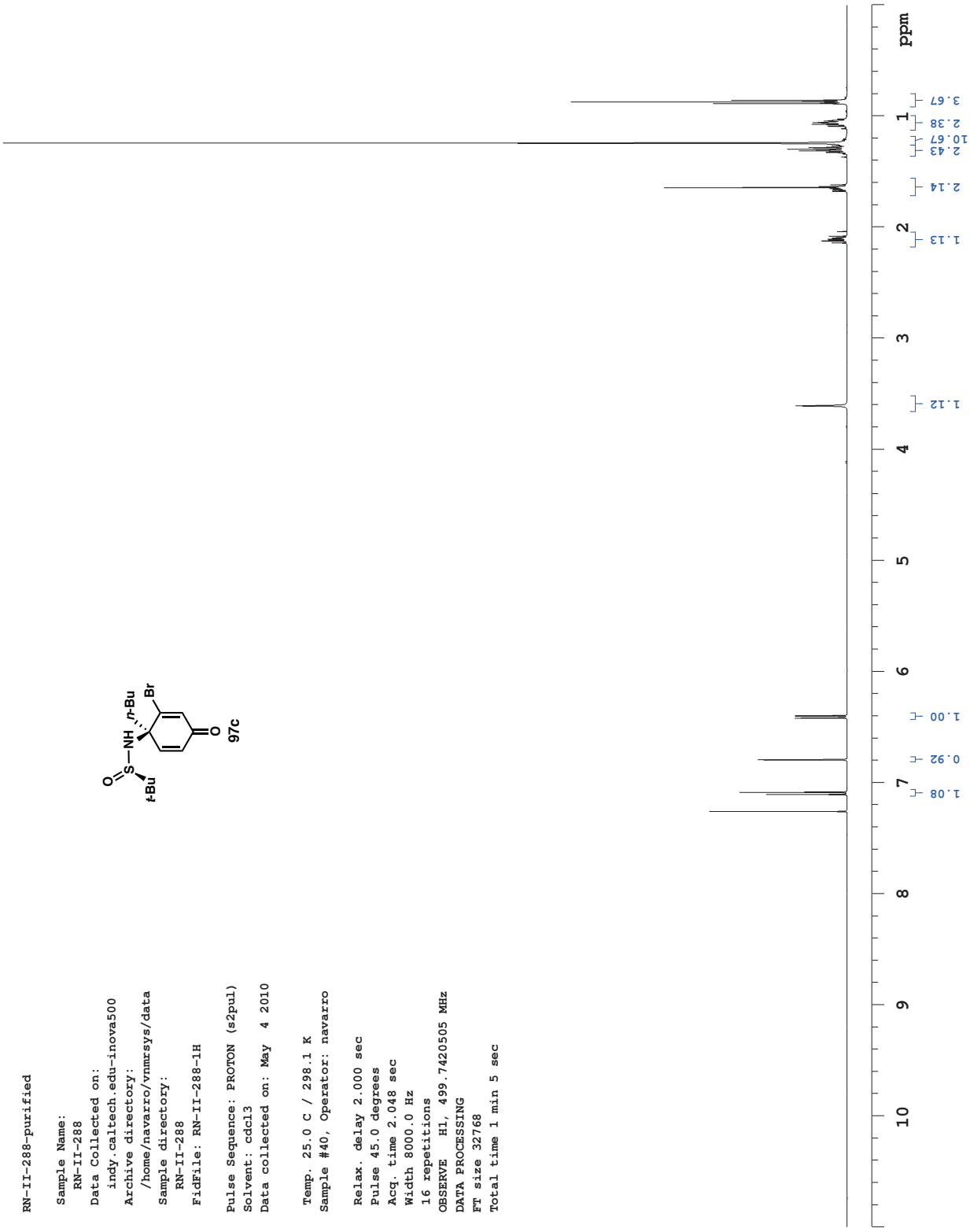

RN-II-287
purified
Sample Name:
RN-II-287
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-II-287
FidFile: RN-II-287-carbon
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 26 2010
Temp. 25.0 C / 298.1 K
Sample #46, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
900 repetitions
OBSERVE C13, 125.6602404 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 30 min
O
S
NH
t-Bu
n-Bu
Cl
O
97a
200
180
160
140
120
100
80
60
40
20
ppm

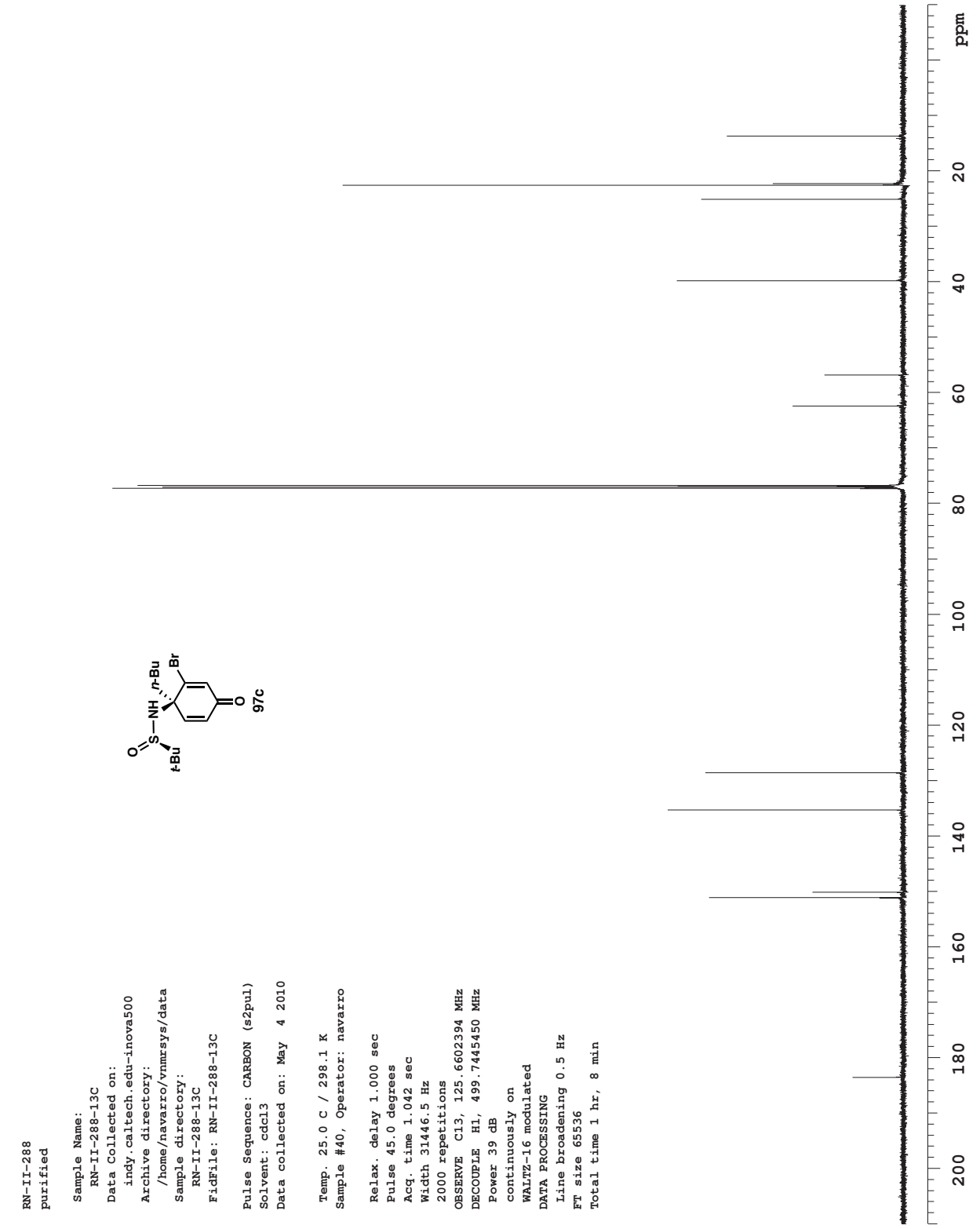

RN-II-292
major product
Sample Name:
RN-II-292-A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-II-292-A
FidFile: RN-II-292-major-1H
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 30 2010
Temp. 25.0 C / 298.1 K
Sample #41, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 32768
Total time 1 min 5 sec
(R,R)-97b
ppm
10.62
1.07
1.00
0.88
1.03
5.43

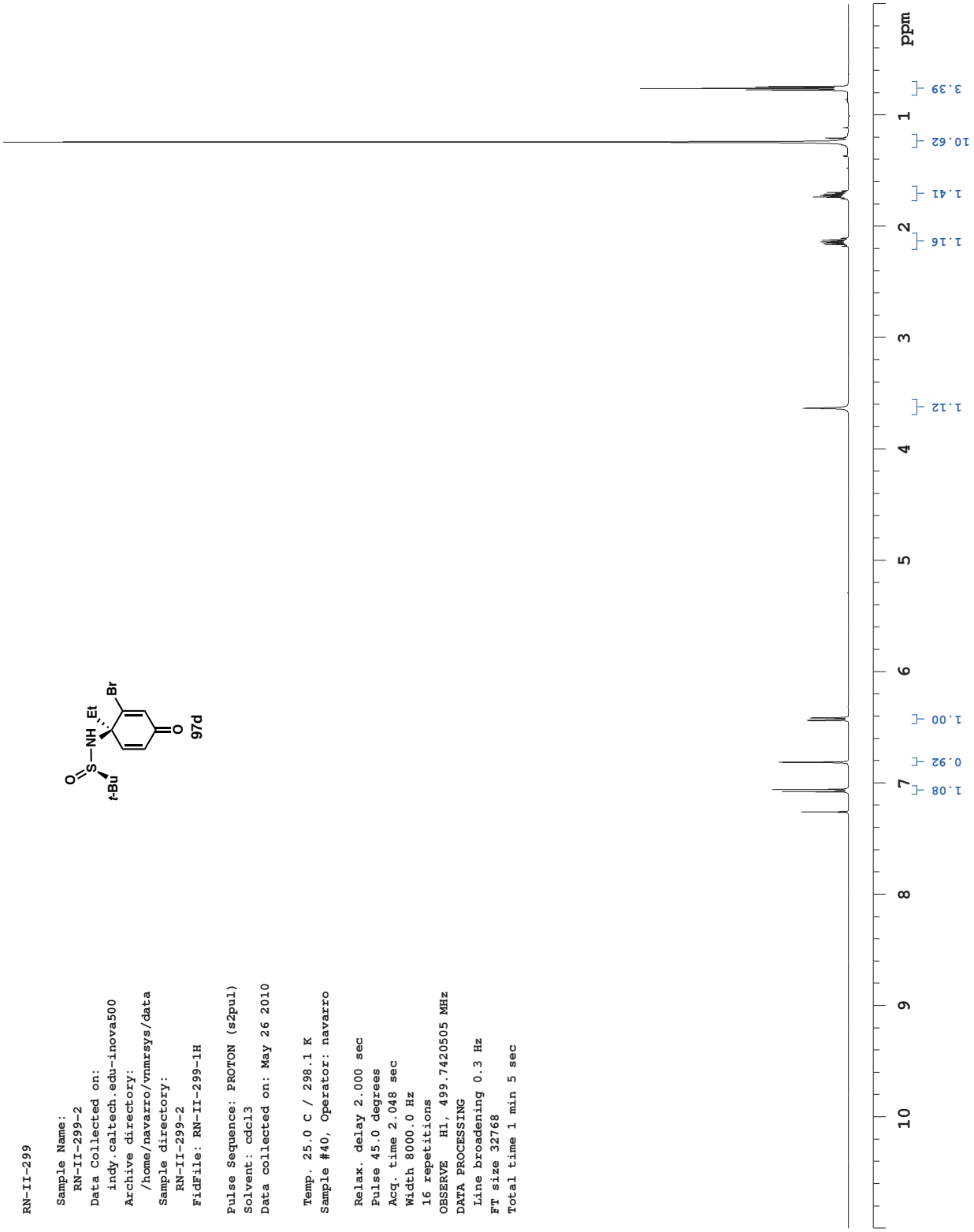

RN-III-54
purified
Sample Name:
RN-III-54
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-54
FidFile: CARBON02
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 20 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1400 repetitions
OBSERVE C13, 125.6602414 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 47 min
O
S
NH
Ph
Cl
t-Bu
O
(R,R)-97b
200
180
160
140
120
100
80
60
40
20
ppm

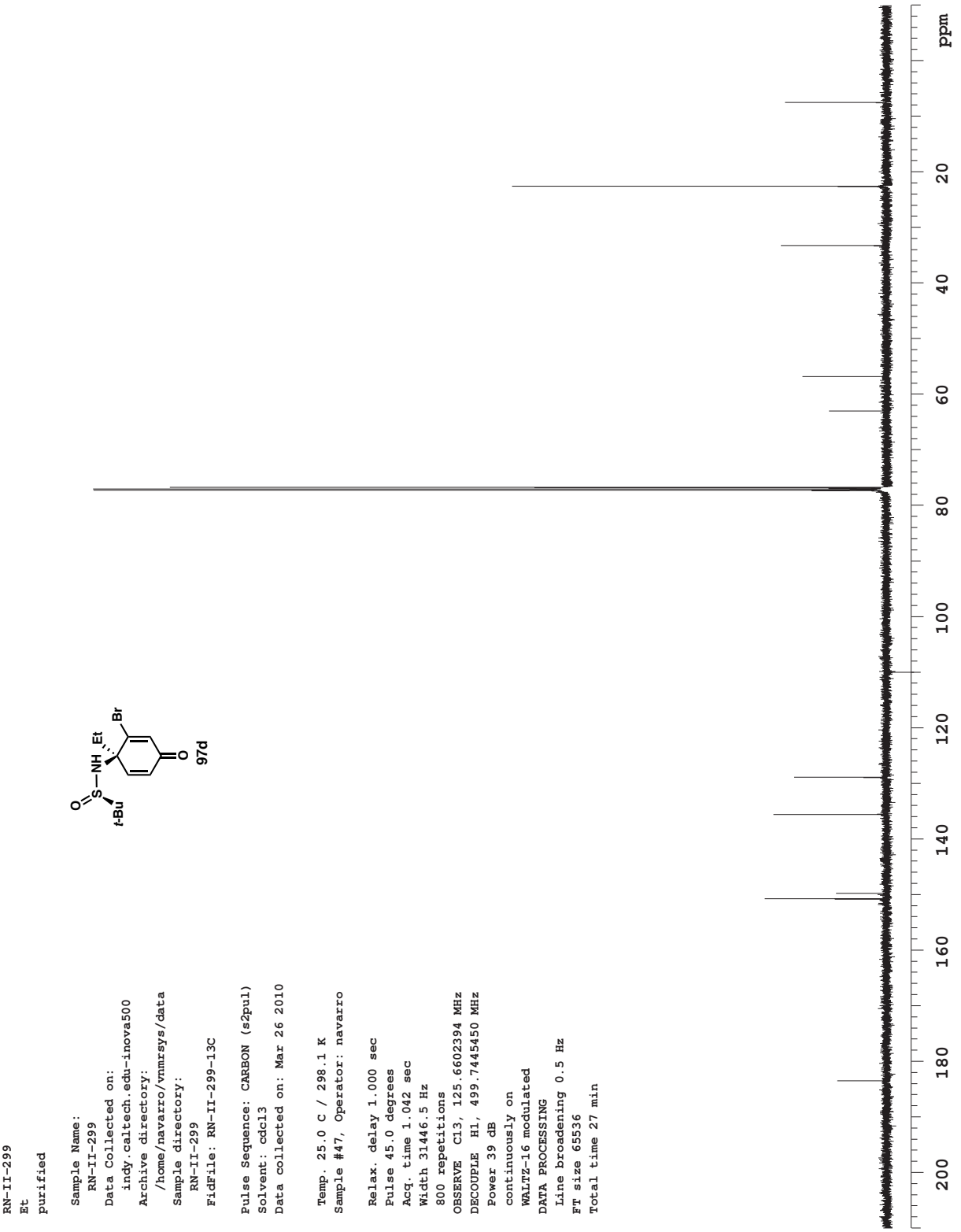

RN-III-54
minor
Sample Name:
RN-III-54-minor
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-54-minor
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 6 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 32768
Total time 1 min 5 sec
(R,S)-97b
ppm
10.55
1.06
1.00
1.04
0.87
5.47

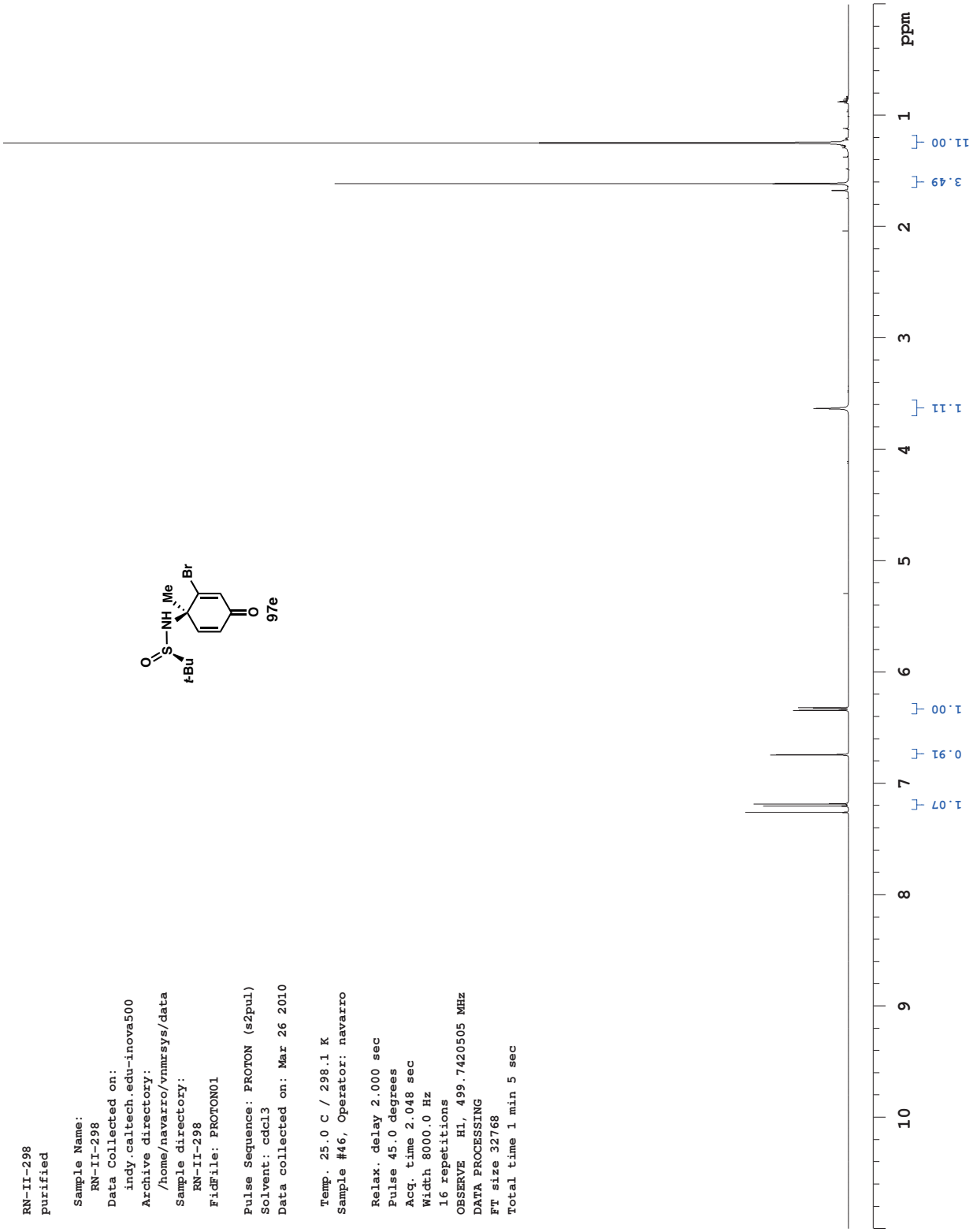

RN-III-54
minor
Sample Name:
RN-III-54-minor
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-54-minor
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 6 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
3100 repetitions
OBSERVE C13, 125.6602385 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 45 min
O
S
NH
Ph
Cl
t-Bu
O
(R,S)-97b
200
180
160
140
120
100
80
60
40
20
ppm

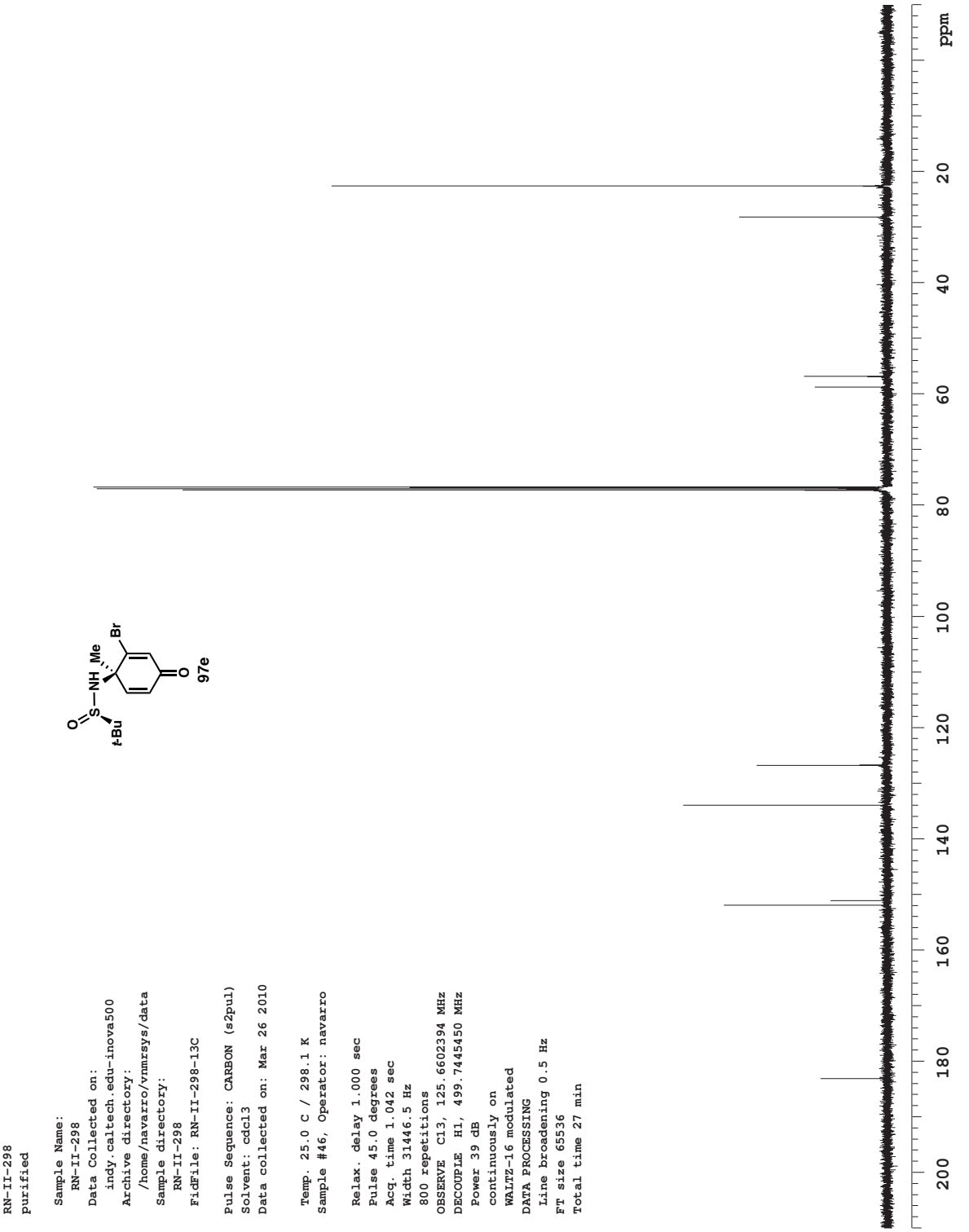

RN-II-288-purified
Sample Name:
RN-II-288
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-II-288
FidFile: RN-II-288-1H
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 4 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 32768
Total time 1 min 5 sec
97c
ppm
3.67
2.38
10.67
2.43
2.14
1.13
1.12
1.00
0.92
1.08

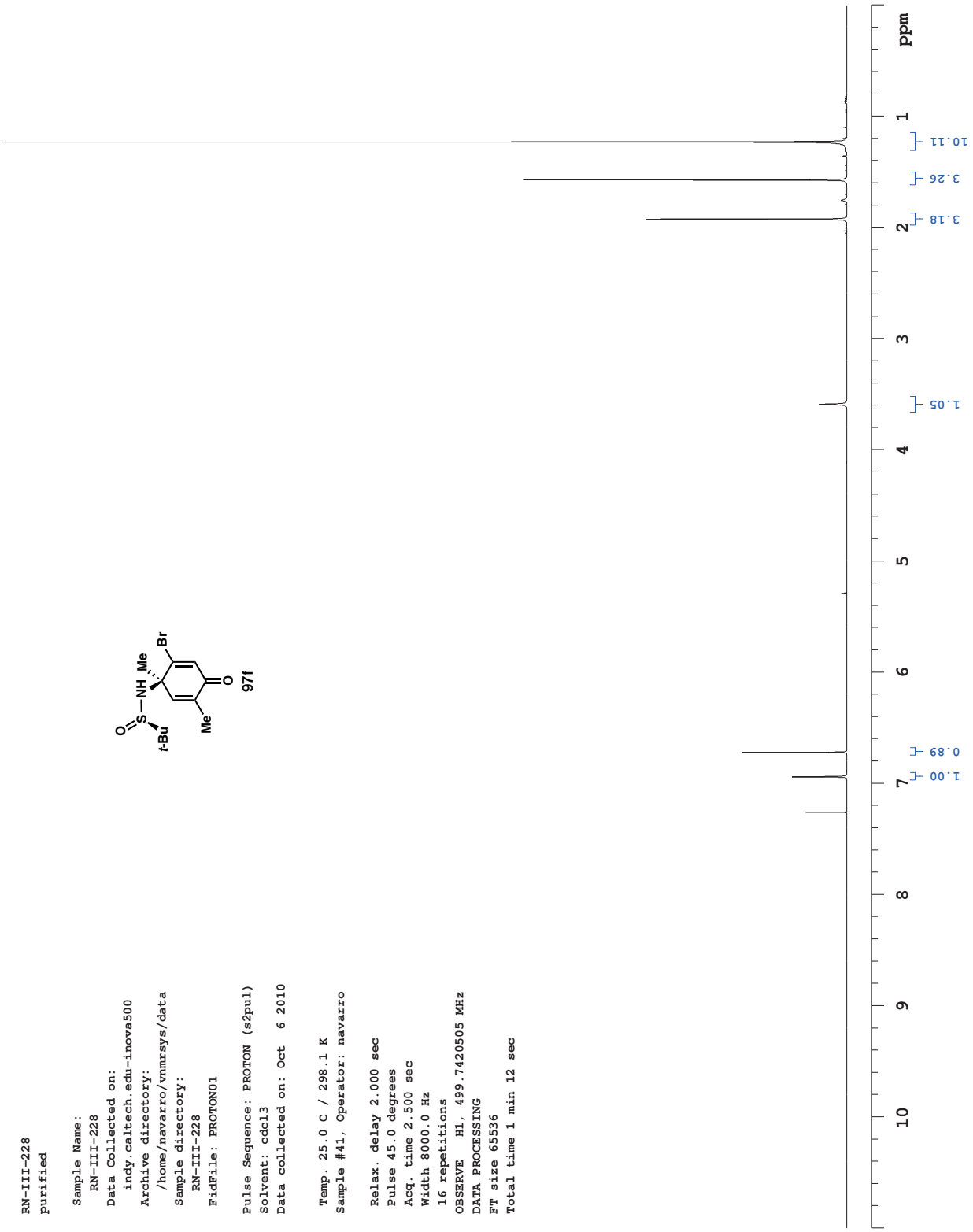

RN-II-288
purified
Sample Name:
RN-II-288-13C
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-II-288-13C
FidFile: RN-II-288-13C
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 4 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2000 repetitions
OBSERVE C13, 125.6602394 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 8 min
t-Bu
Br
NH
S
O
t-Bu
O
97c
200
180
160
140
120
100
80
60
40
20
ppm

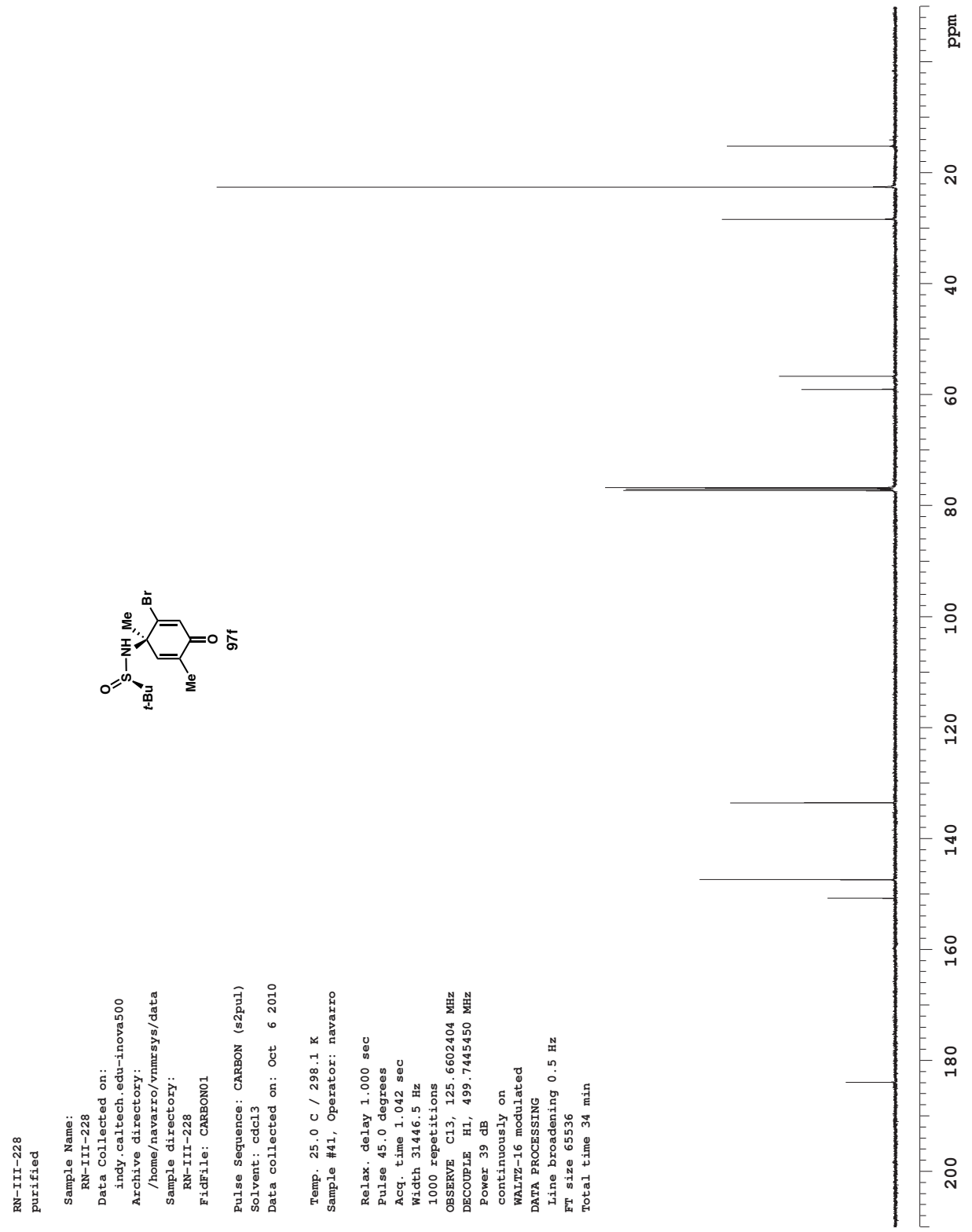

RN-II-299
Sample Name:
RN-II-299-2
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-II-299-2
FidFile: RN-II-299-1H
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 26 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
Line broadening 0.3 Hz
FT size 32768
Total time 1 min 5 sec
Br
Et
NH
S
O
O
t-Bu
O
97d
ppm
10
9
8
7
6
5
4
3
2
1
1.08
0.92
1.00
1.12
1.16
1.41
10.62
3.39

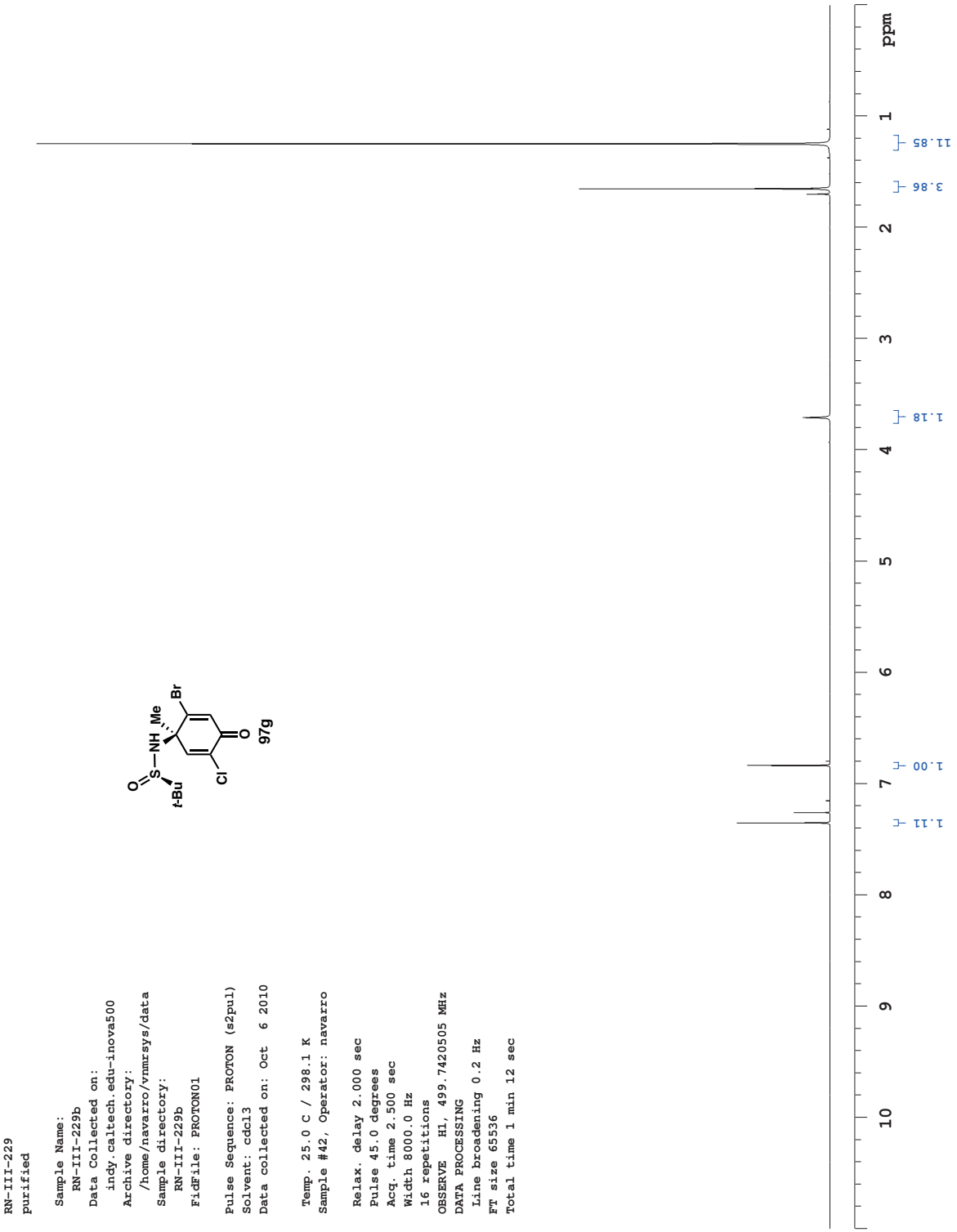

RN-II-299
Et
purified
Sample Name:
RN-II-299
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-II-299
FidFile: RN-II-299-13C
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 26 2010
Temp. 25.0 C / 298.1 K
Sample #47, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
800 repetitions
OBSERVE C13, 125.6602394 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 27 min
Br
Et
NH
S
O
t-Bu
O
97d
200
180
160
140
120
100
80
60
40
20
ppm

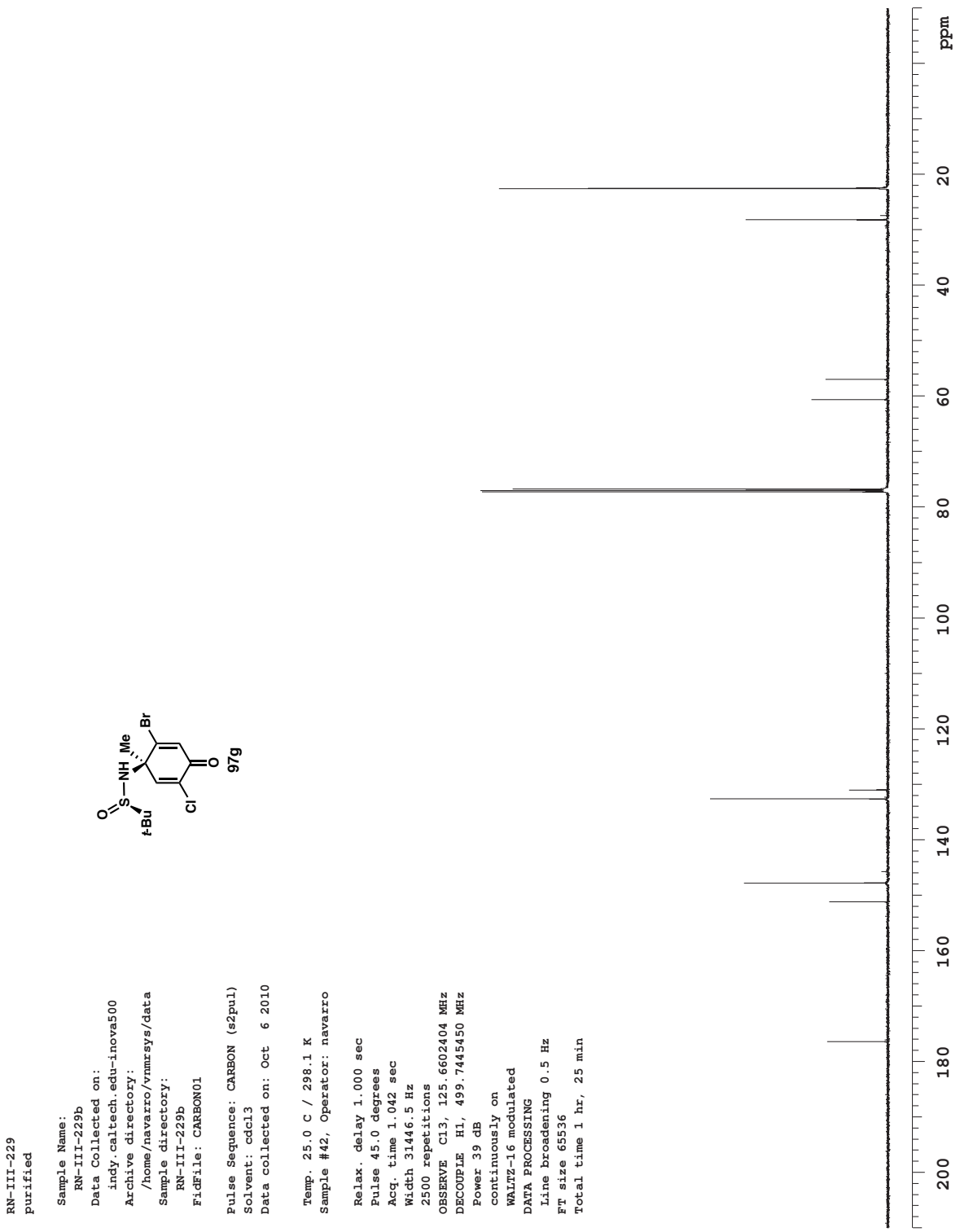

RN-II-298
purified
Sample Name:
RN-II-298
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-II-298
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 26 2010
Temp. 25.0 C / 298.1 K
Sample #46, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 32768
Total time 1 min 5 sec
O
S
NH
Me
Br
t-Bu
O
97e
ppm
10
9
8
7
6
5
4
3
2
1
1.07
0.91
1.00
1.11
3.49
11.00

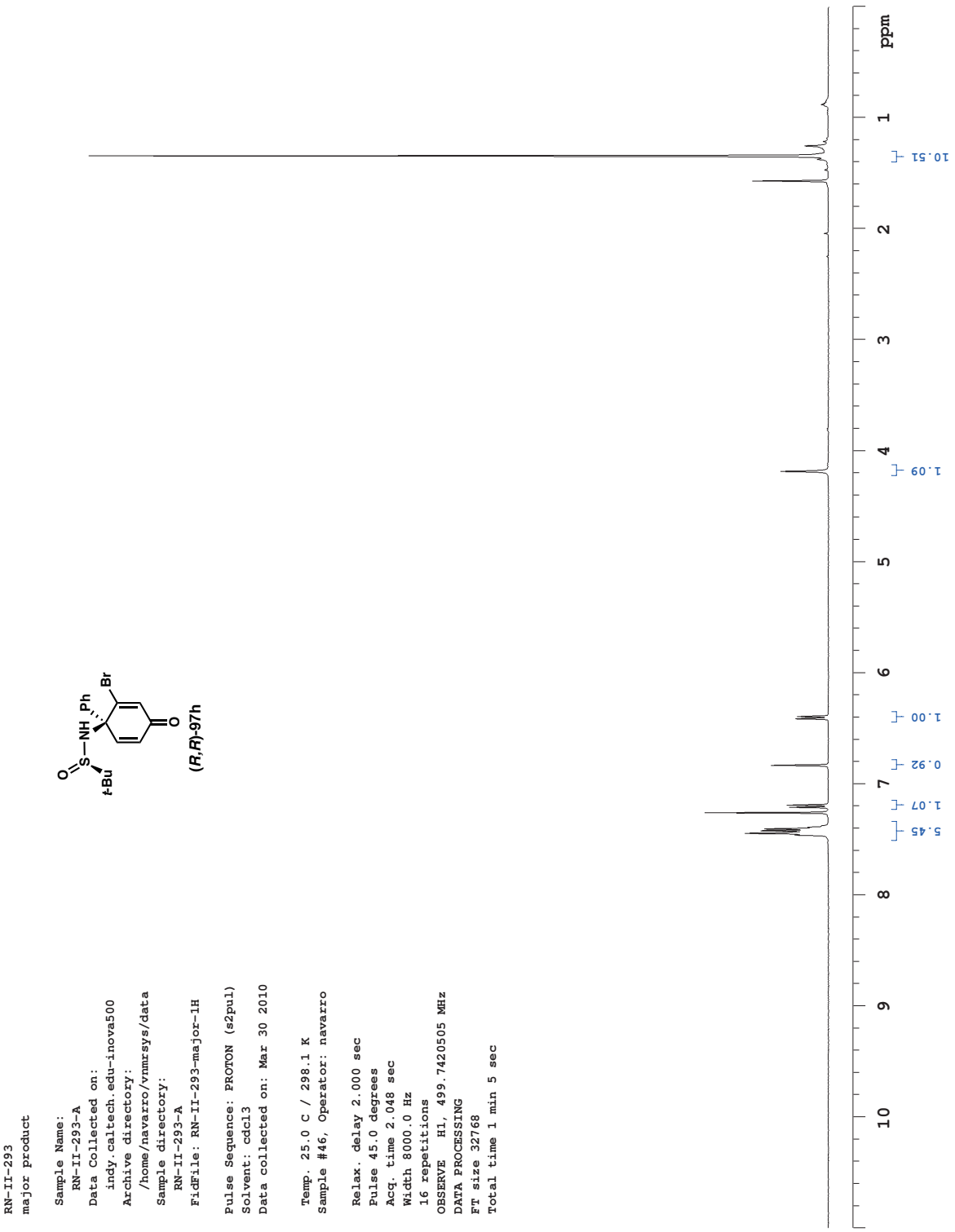

RN-II-298
purified
Sample Name:
RN-II-298
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-II-298
FidFile: RN-II-298-13C
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 26 2010
Temp. 25.0 C / 298.1 K
Sample #46, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
800 repetitions
OBSERVE C13, 125.6602394 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 27 min
O
S
NH
Me
Br
t-Bu
O
97e
200
180
160
140
120
100
80
60
40
20
ppm

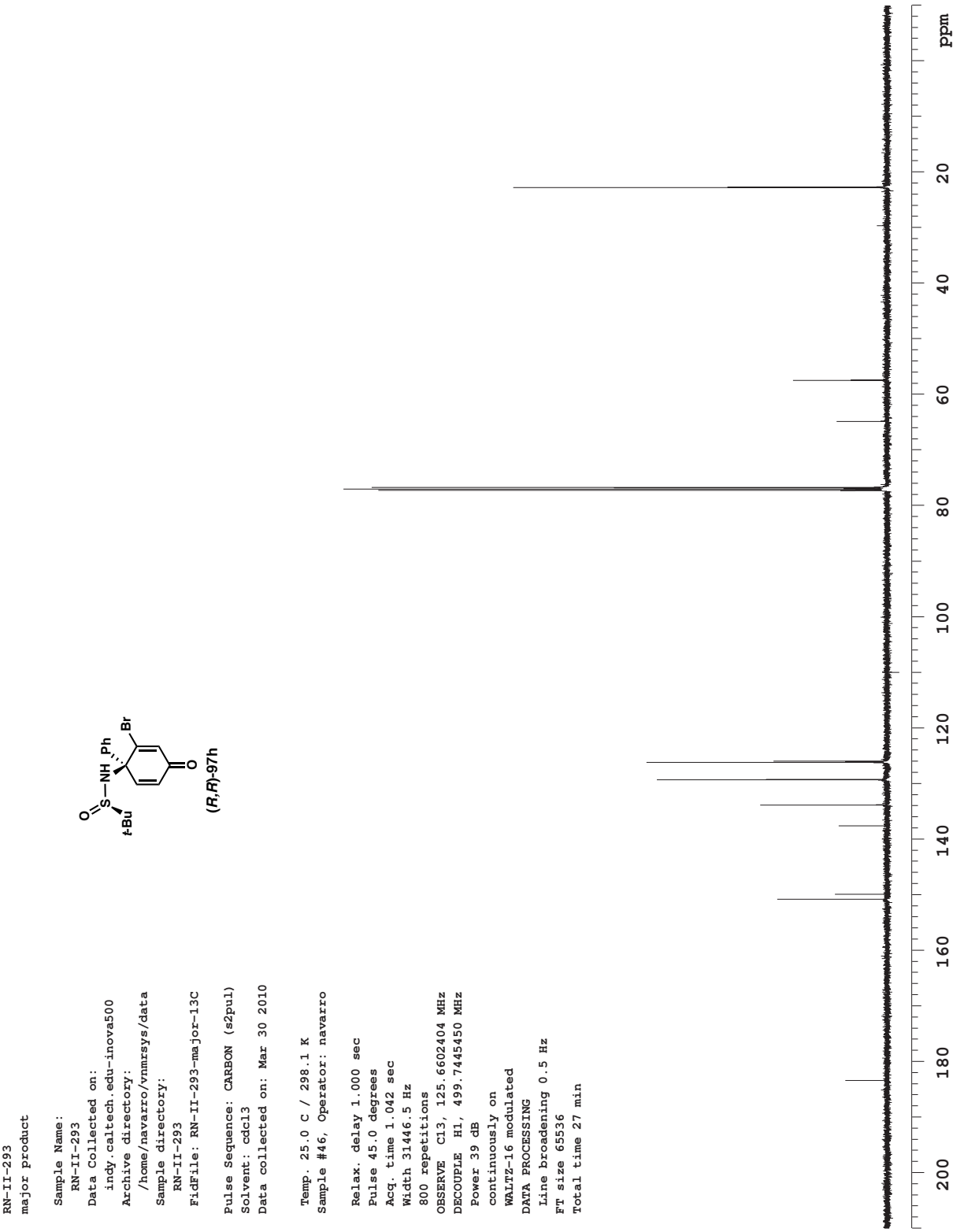

RN-III-228
purified
Sample Name:
RN-III-228
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-228
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 6 2010
Temp. 25.0 C / 298.1 K
Sample #41, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 65536
Total time 1 min 12 sec
Br
Me
NH
Me
O
S
O
t-Bu
Me
O
97f
10.11
3.26
3.18
1.05
0.89
1.00
ppm
10
9
8
7
6
5
4
3
2
1

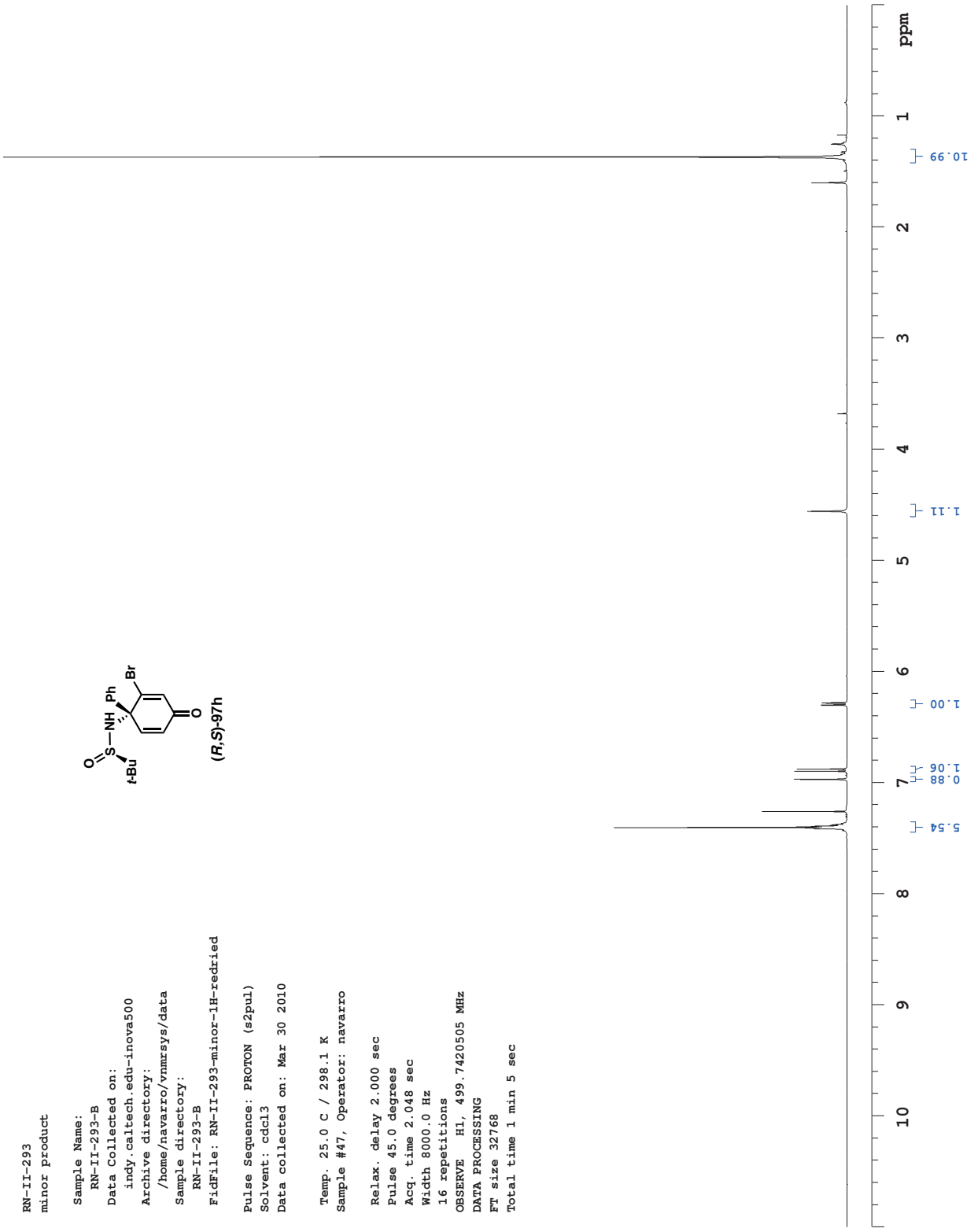

RN-III-228
purified
Sample Name:
RN-III-228
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-228
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 6 2010
Temp. 25.0 C / 298.1 K
Sample #41, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6602404 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
Me
NH
S
O
t-Bu
Br
O
Me
97f
200
180
160
140
120
100
80
60
40
20
ppm


RN-III-229
purified
Sample Name:
RN-III-229b
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-229b
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 6 2010
Temp. 25.0 C / 298.1 K
Sample #42, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 1 min 12 sec
Br
Me
NH
S
O
t-Bu
Cl
O
97g
11.85
3.86
1.18
1.00
1.11
ppm
10
9
8
7
6
5
4
3
2
1


RN-III-229
purified
Sample Name:
RN-III-229b
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-229b
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 6 2010
Temp. 25.0 C / 298.1 K
Sample #42, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2500 repetitions
OBSERVE C13, 125.6602404 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 25 min
97g
ppm
200
180
160
140
120
100
80
60
40
20


RN-II-293
major product
Sample Name:
RN-II-293-A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-II-293-A
FidFile: RN-II-293-major-1H
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 30 2010
Temp. 25.0 C / 298.1 K
Sample #46, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 32768
Total time 1 min 5 sec
Br
Ph
NH
S
O
O
t-Bu
O
(R,R)-97h
10.51
1.09
1.00
0.92
1.07
5.45
ppm
1
2
3
4
5
6
7
8
9
10


RN-II-293
major product
Sample Name:
RN-II-293
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-II-293
FidFile: RN-II-293-major-13C
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 30 2010
Temp. 25.0 C / 298.1 K
Sample #46, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
800 repetitions
OBSERVE C13, 125.6602404 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 27 min
Br
Ph
NH
S
O
O
t-Bu
O
(R,R)-97h
200
180
160
140
120
100
80
60
40
20
ppm


RN-II-293
minor product
Sample Name:
RN-II-293-B
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-II-293-B
FidFile: RN-II-293-minor-1H-redried
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 30 2010
Temp. 25.0 C / 298.1 K
Sample #47, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 32768
Total time 1 min 5 sec
O
S
NH
Ph
Br
t-Bu
O
(R,S)-97h
10.99
1.11
1.00
0.88
1.06
5.54
ppm
10
9
8
7
6
5
4
3
2
1

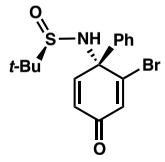
RN-III-293 minor
purified

Sample Name:
RN-II-293-minor
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-II-293-minor
FidFile: CARBON01

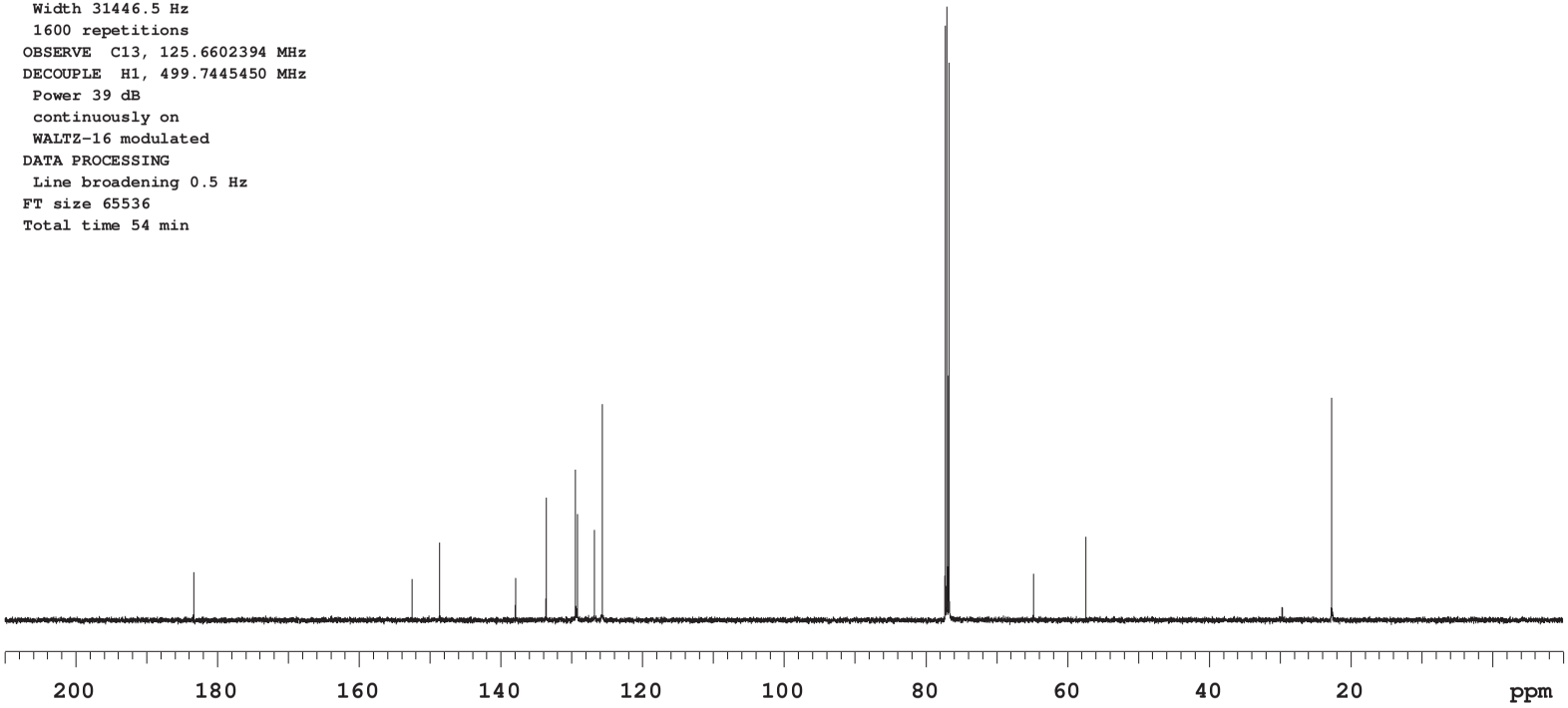
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 20 2010

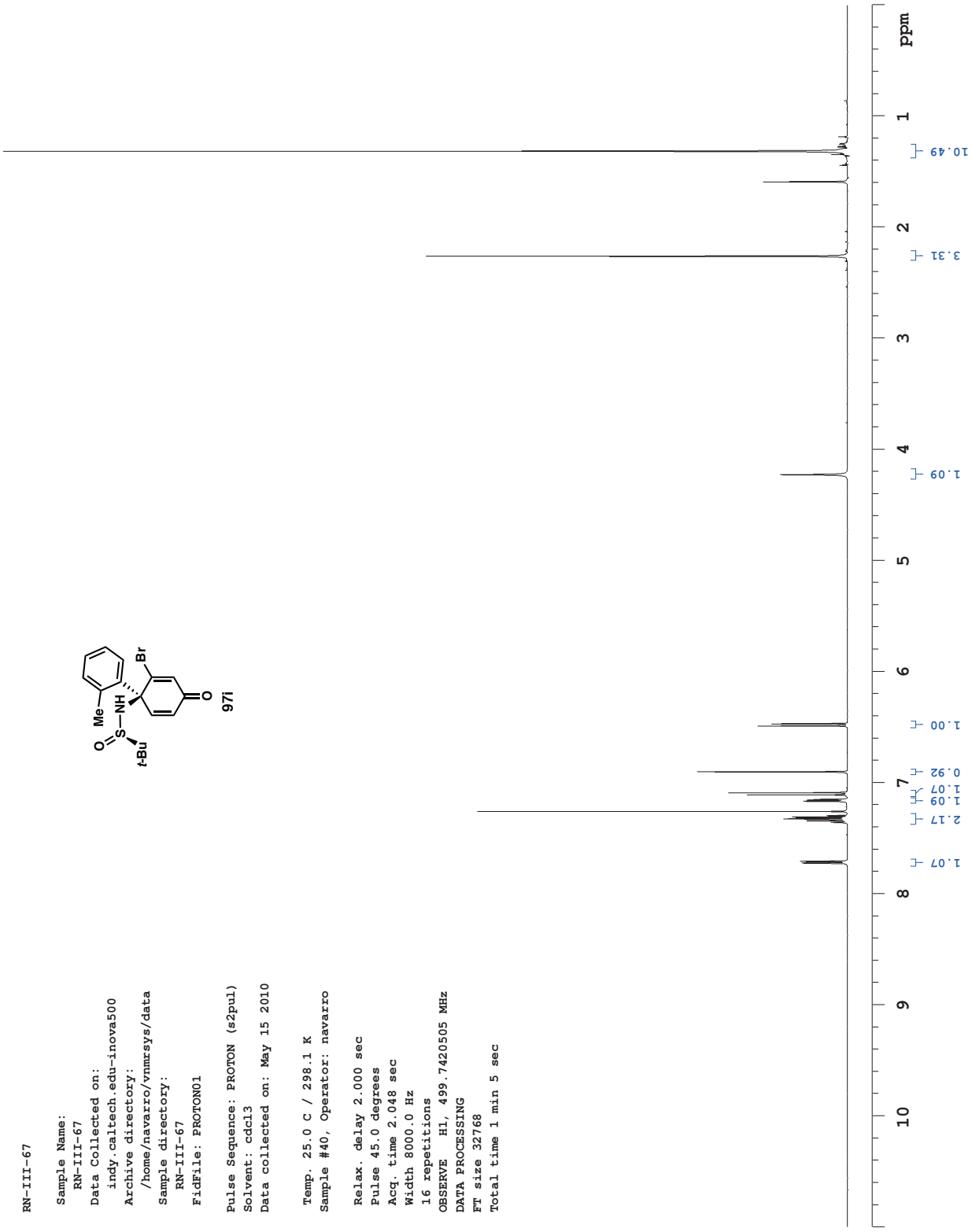
Temp. 25.0 C / 298.1 K
Sample #41, Operator: navarro

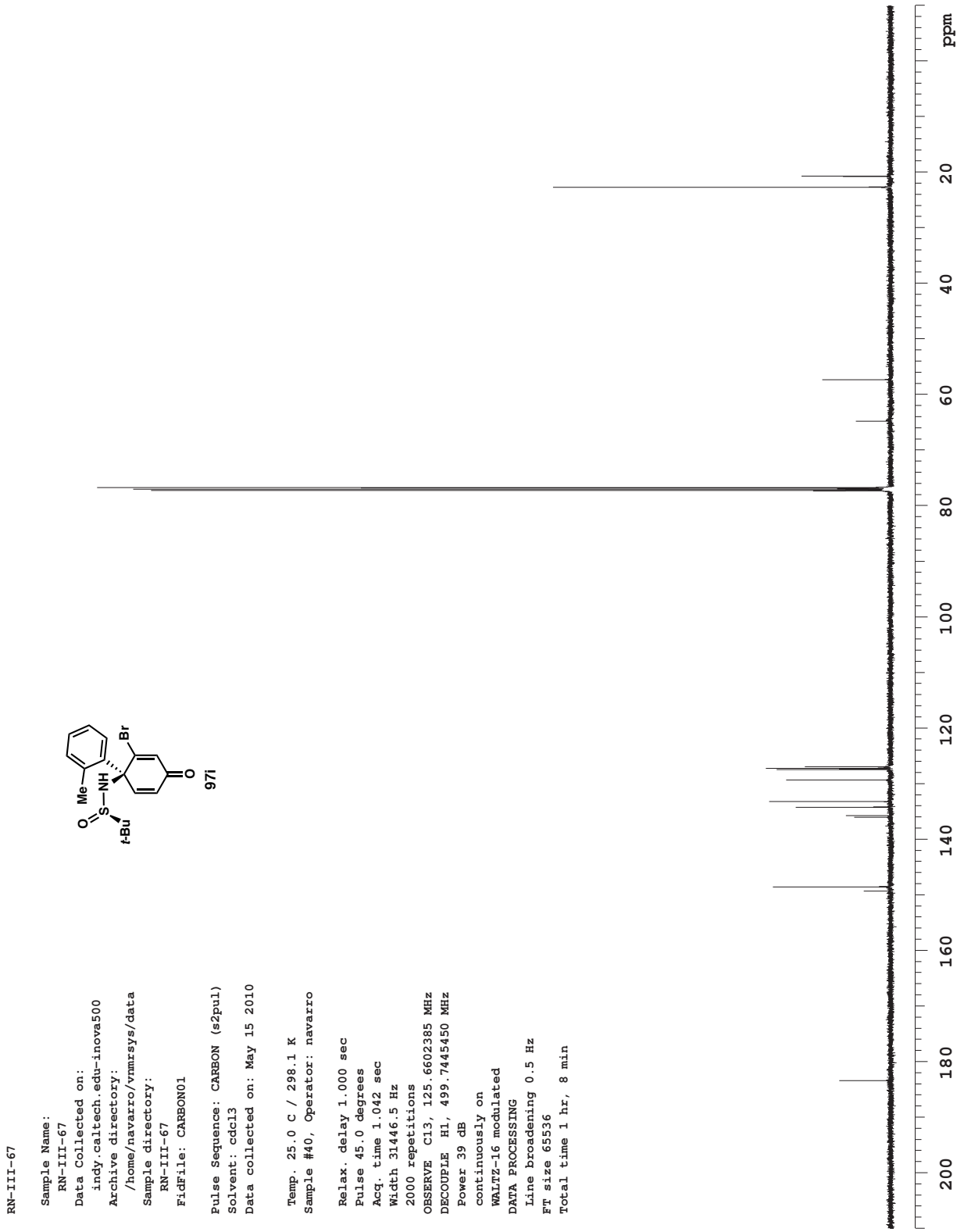
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1600 repetitions
OBSERVE C13, 125.6602394 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 54 min

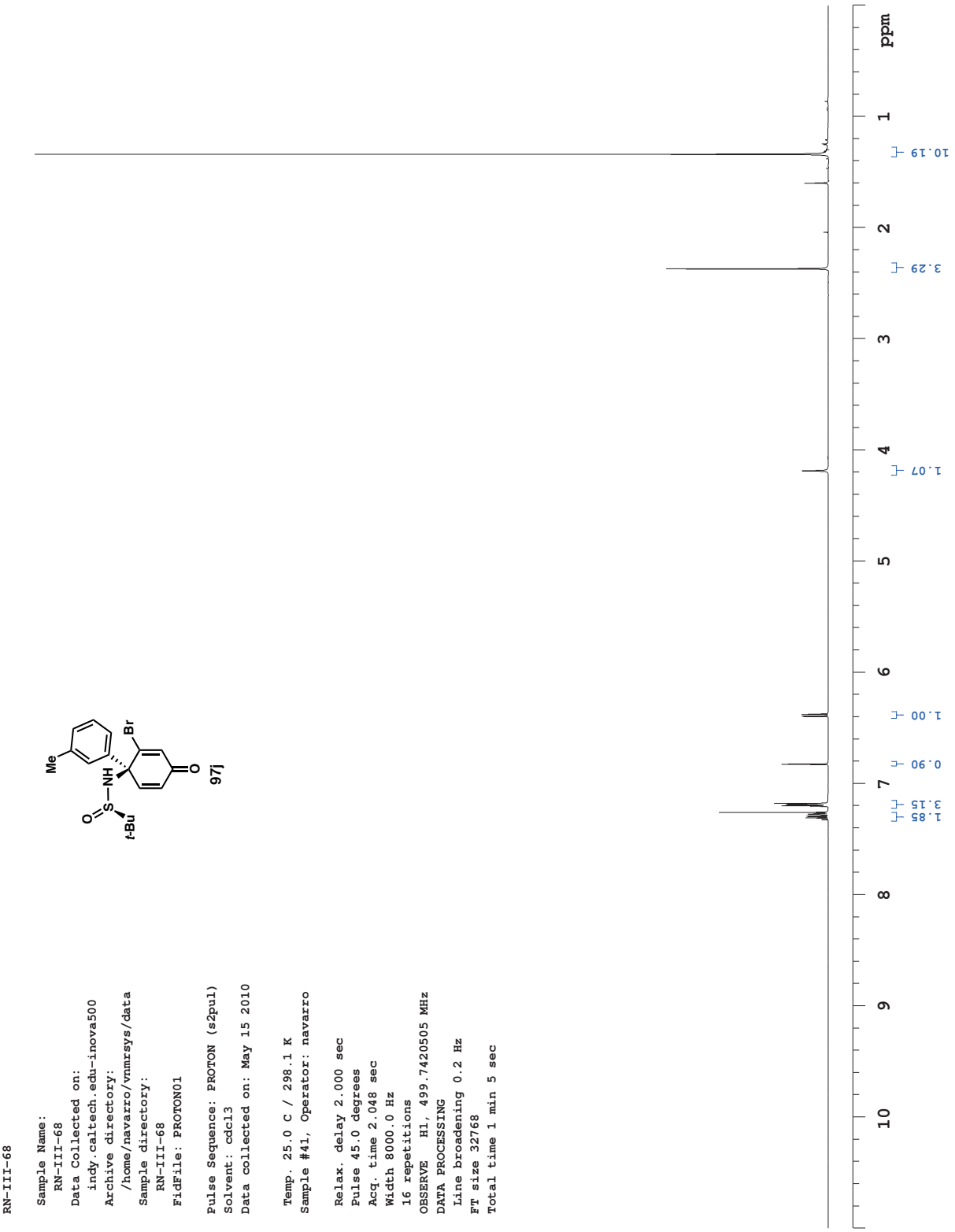


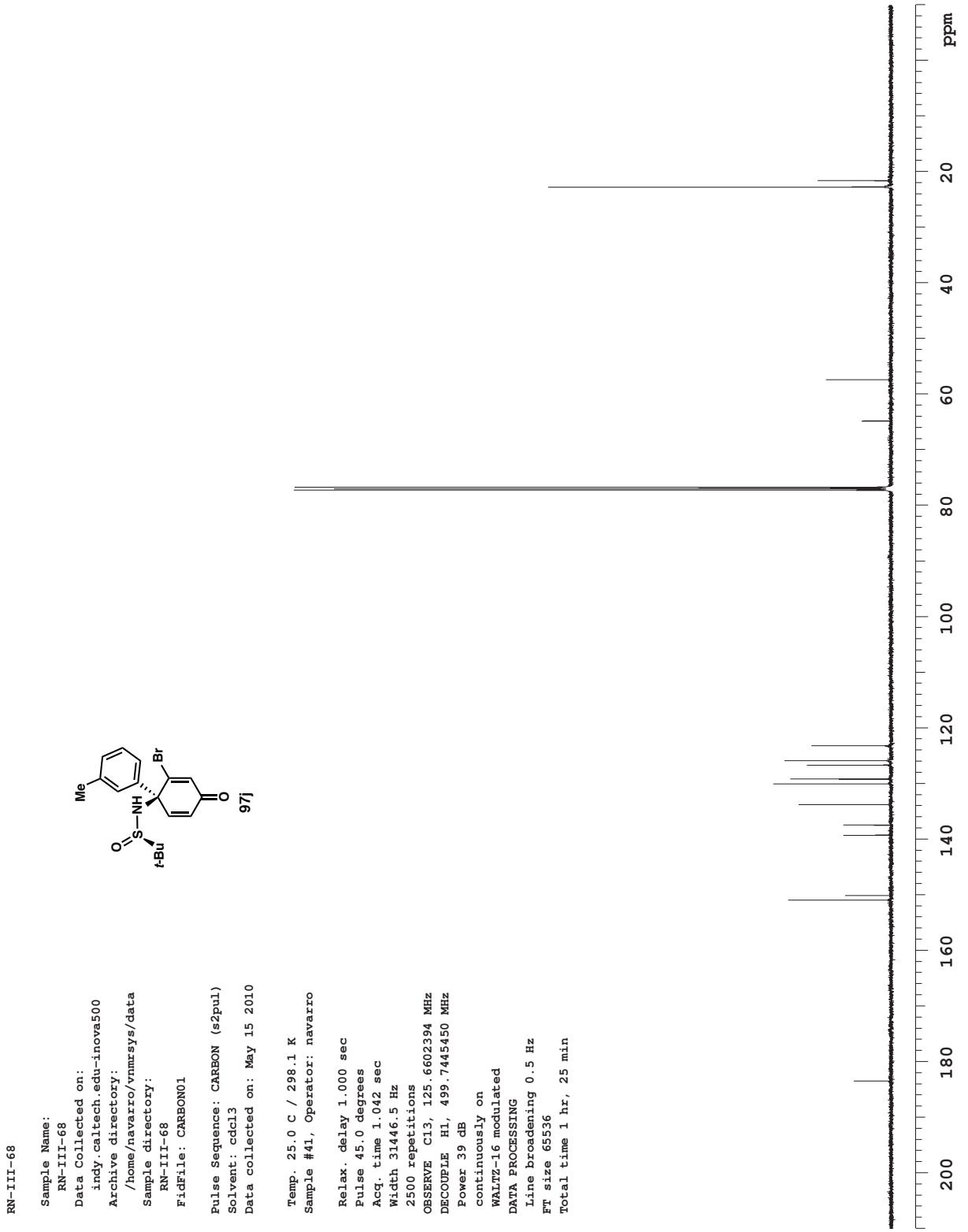
(*R*,*S*)-97h

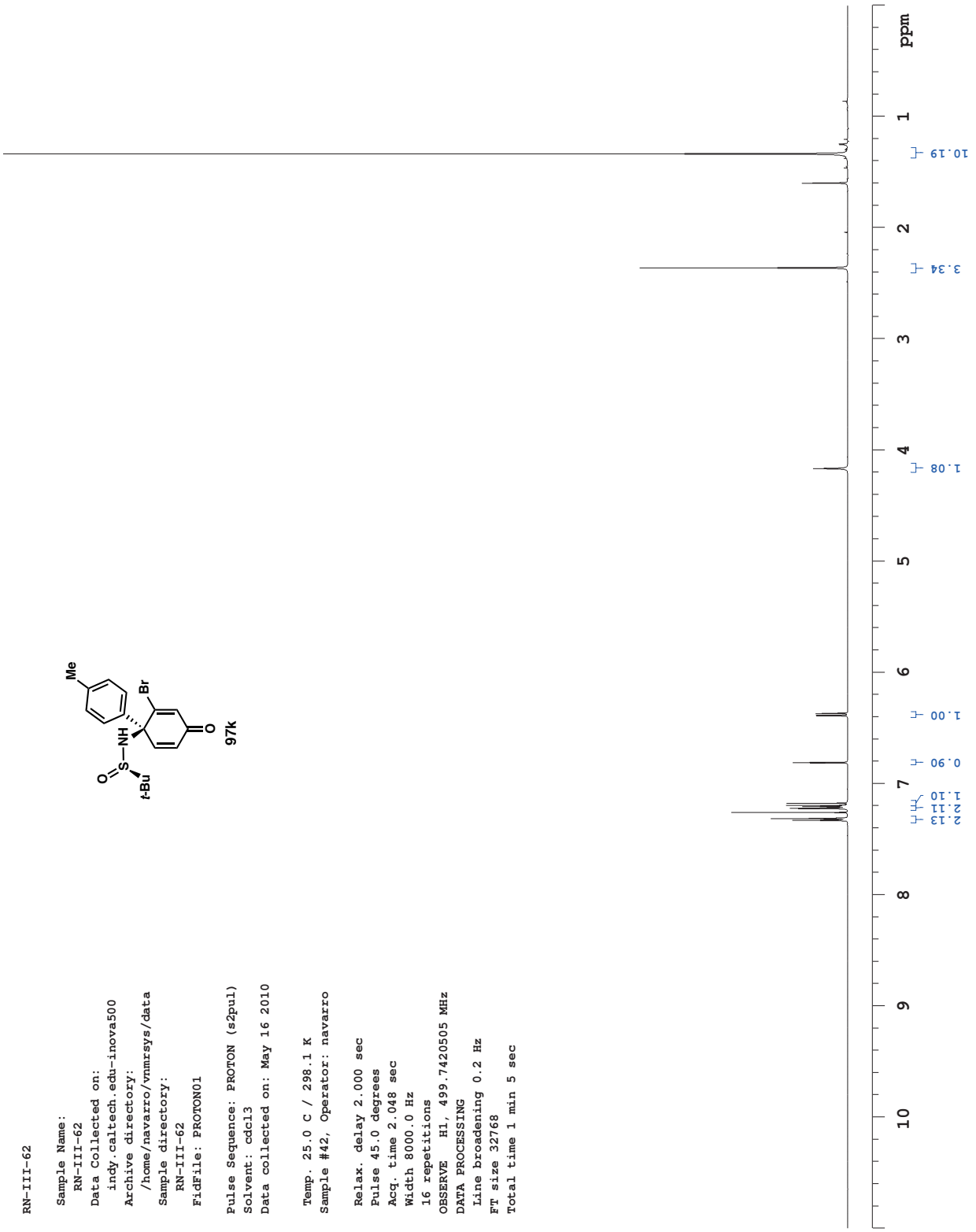


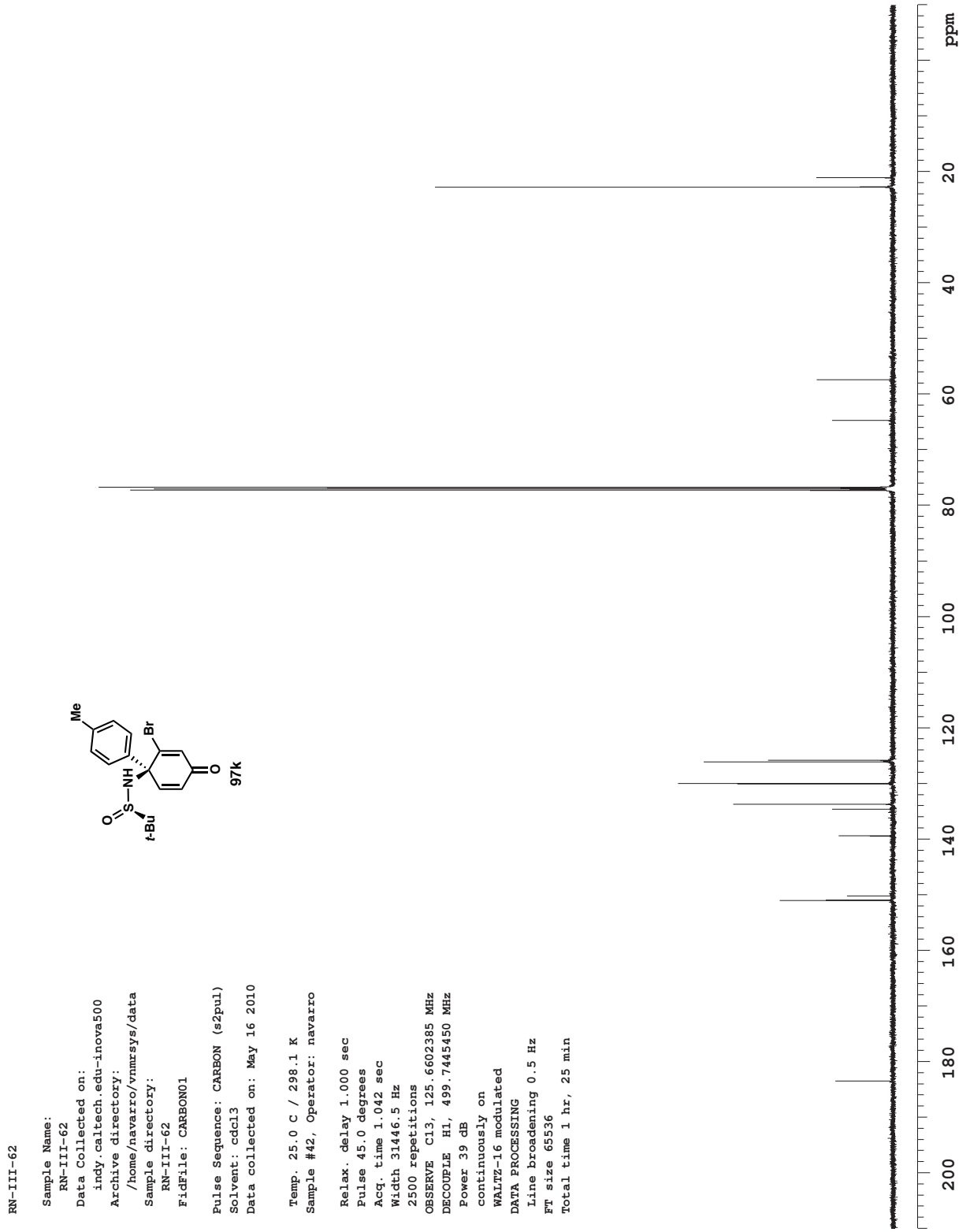

RN-III-67
Sample Name:
RN-III-67
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-67
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 15 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 32768
Total time 1 min 5 sec
Me
NH
S
O
t-Bu
Br
O
97i
ppm
10.49
3.31
1.09
1.00
0.92
1.07
1.09
2.17
1.07

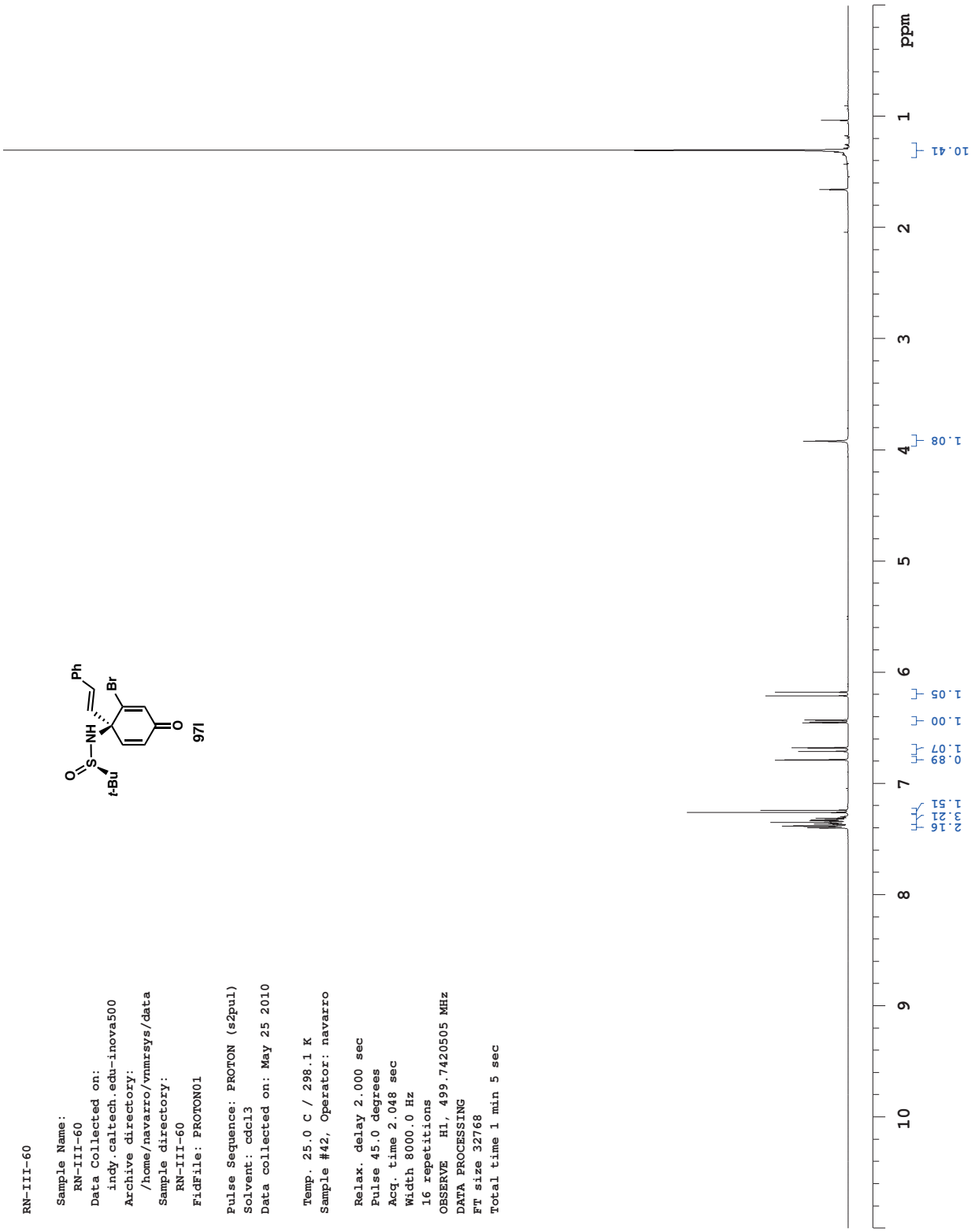

RN-III-67
Sample Name:
RN-III-67
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-67
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 15 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2000 repetitions
OBSERVE C13, 125.6602385 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 8 min
Me
NH
Br
O
S
O
t-Bu
97i
200
180
160
140
120
100
80
60
40
20
ppm

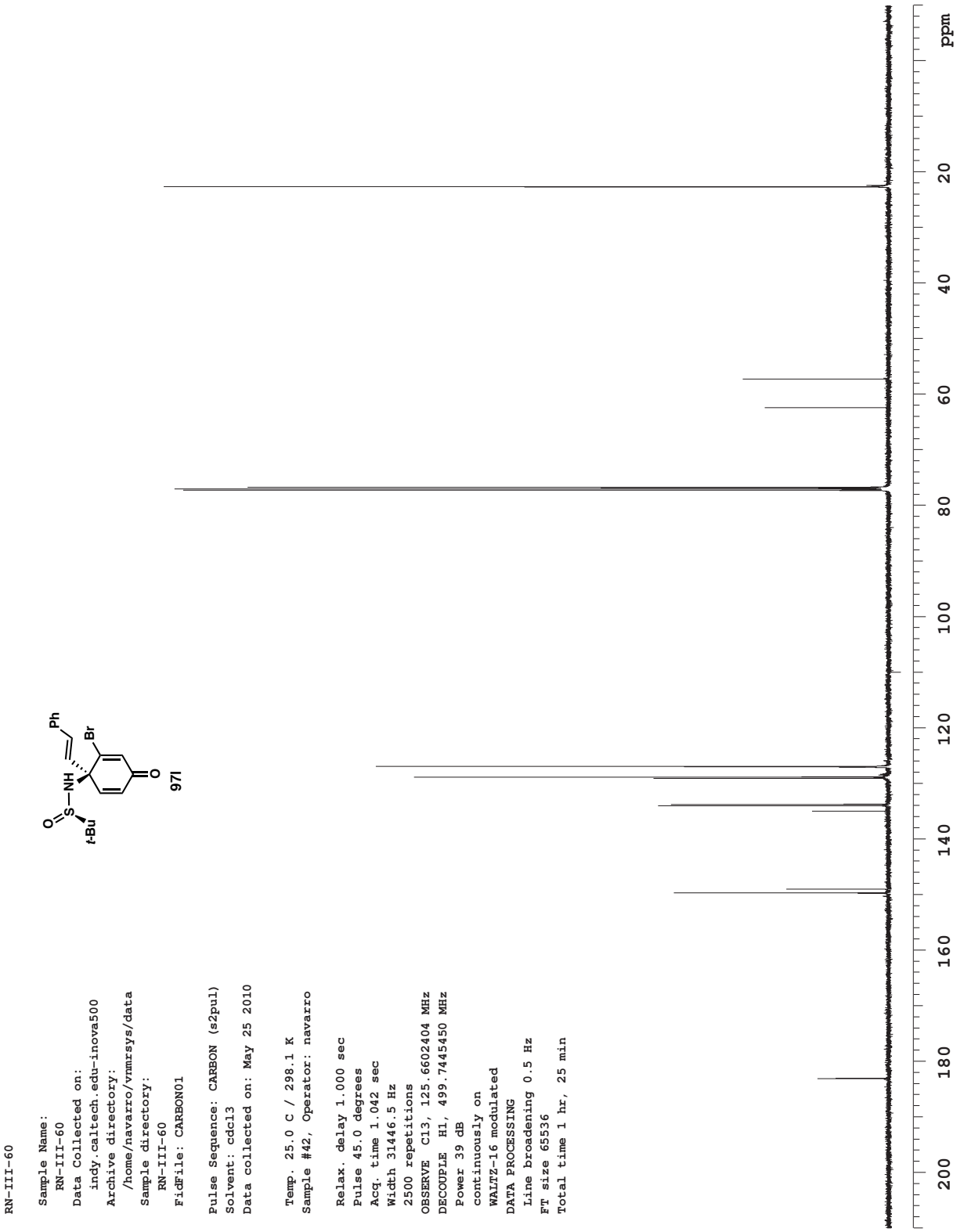

RN-III-68
Sample Name:
RN-III-68
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-68
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 15 2010
Temp. 25.0 C / 298.1 K
Sample #41, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 32768
Total time 1 min 5 sec
Me
Br
NH
S
O
O
t-Bu
O
97j
ppm
10.19
3.29
1.07
1.00
0.90
3.15
1.85

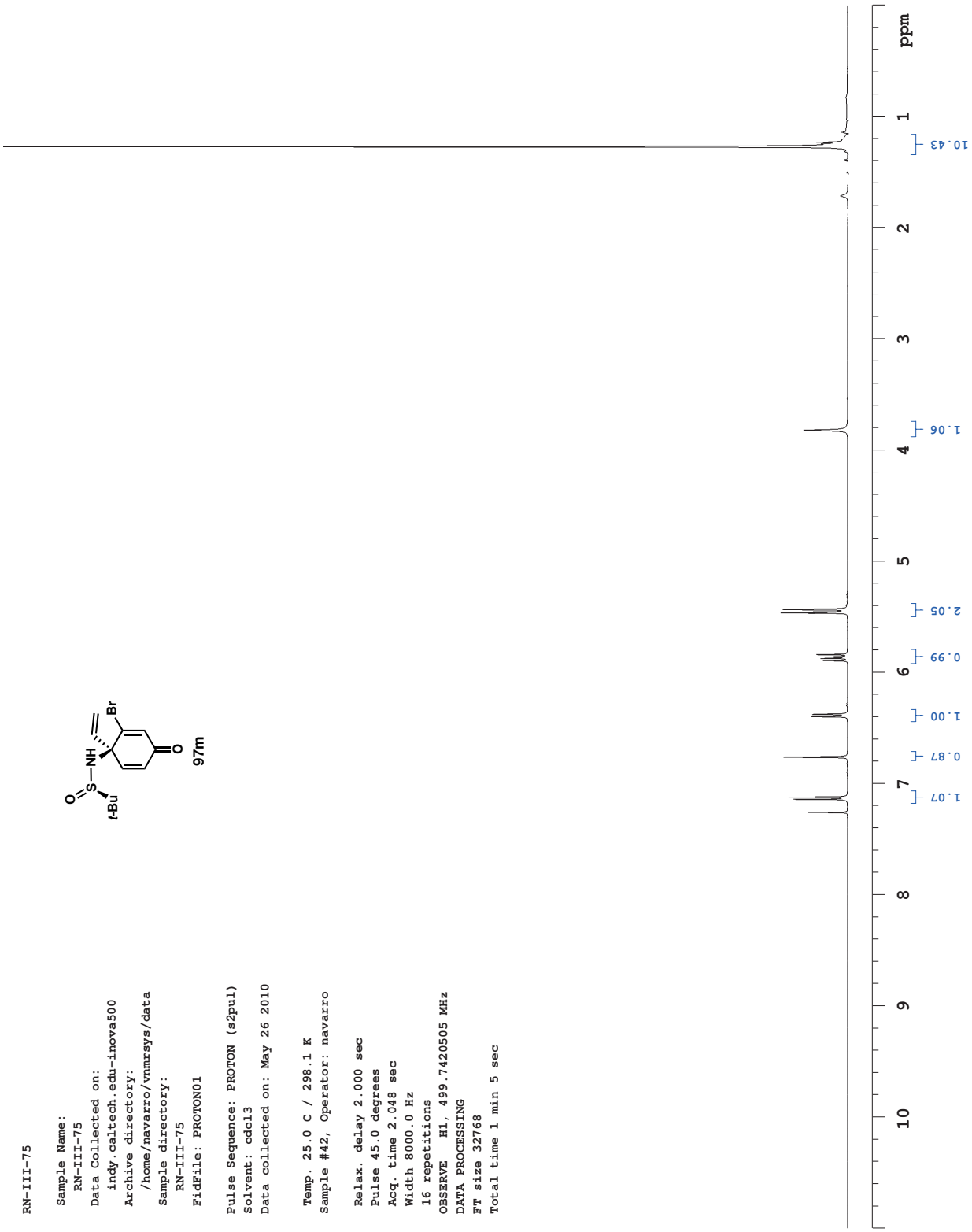

RN-III-68
Sample Name:
RN-III-68
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-68
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 15 2010
Temp. 25.0 C / 298.1 K
Sample #41, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2500 repetitions
OBSERVE C13, 125.6602394 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 25 min
Me
Br
NH
O
S
O
t-Bu
97j
200
180
160
140
120
100
80
60
40
20
ppm

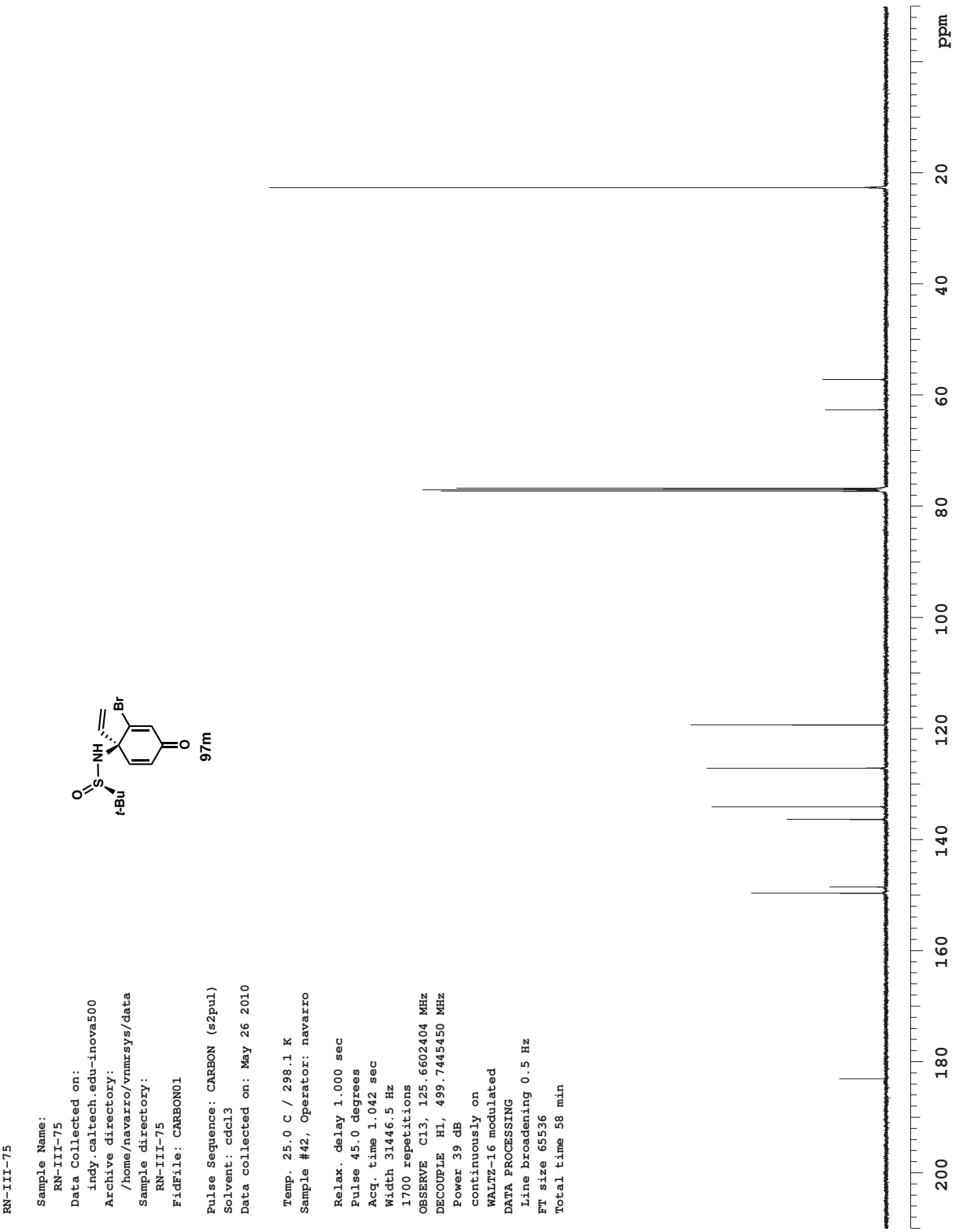

RN-III-62
Sample Name:
RN-III-62
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-62
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 16 2010
Temp. 25.0 C / 298.1 K
Sample #42, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 32768
Total time 1 min 5 sec
Me
Br
NH
S
O
O
t-Bu
O
97k
ppm
10.19
3.34
1.08
1.00
0.90
1.10
2.11
2.13

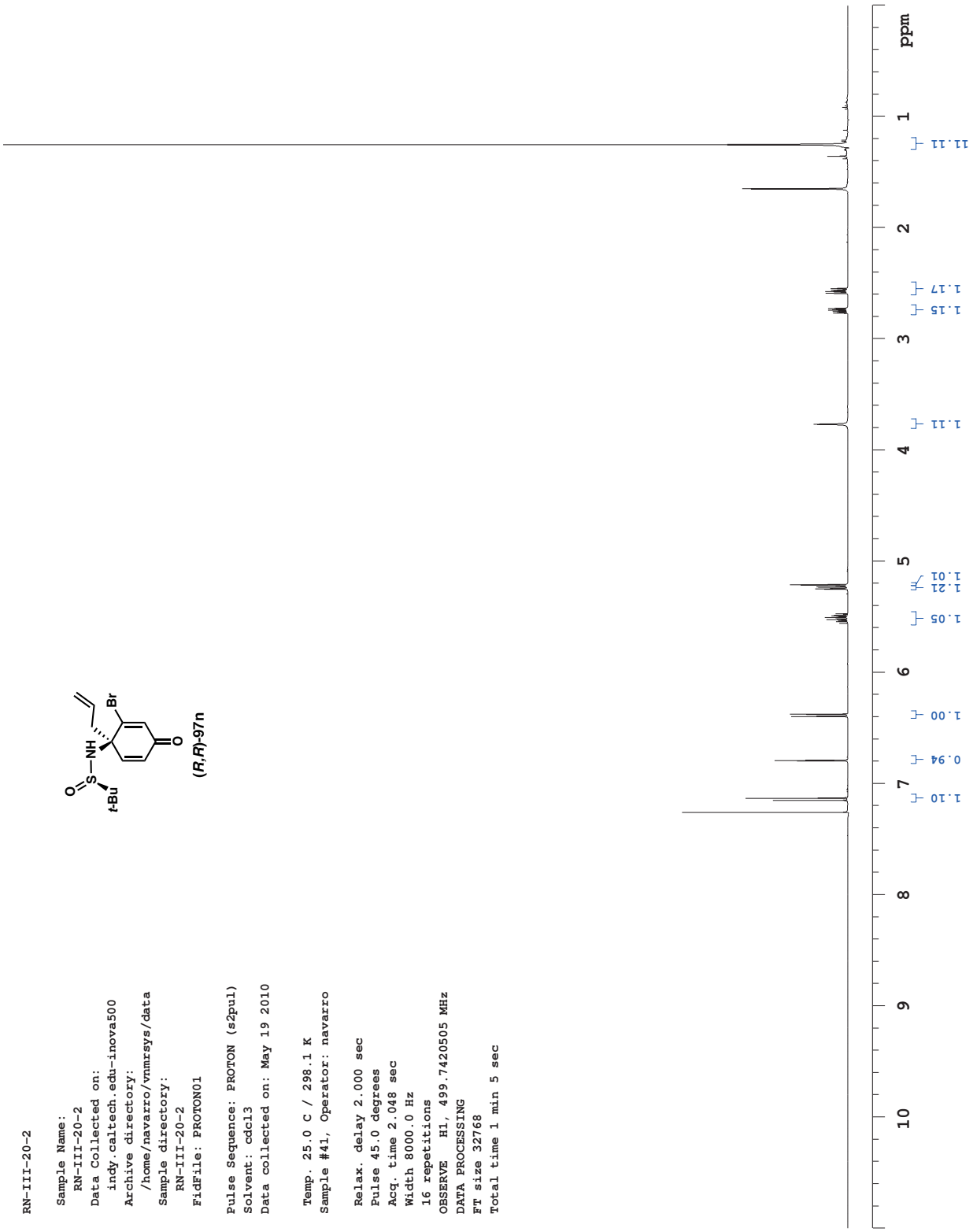

RN-III-62
Sample Name:
RN-III-62
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-62
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 16 2010
Temp. 25.0 C / 298.1 K
Sample #42, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2500 repetitions
OBSERVE C13, 125.6602385 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 25 min
Me
Br
NH
S
O
O
t-Bu
O
97k
200
180
160
140
120
100
80
60
40
20
ppm

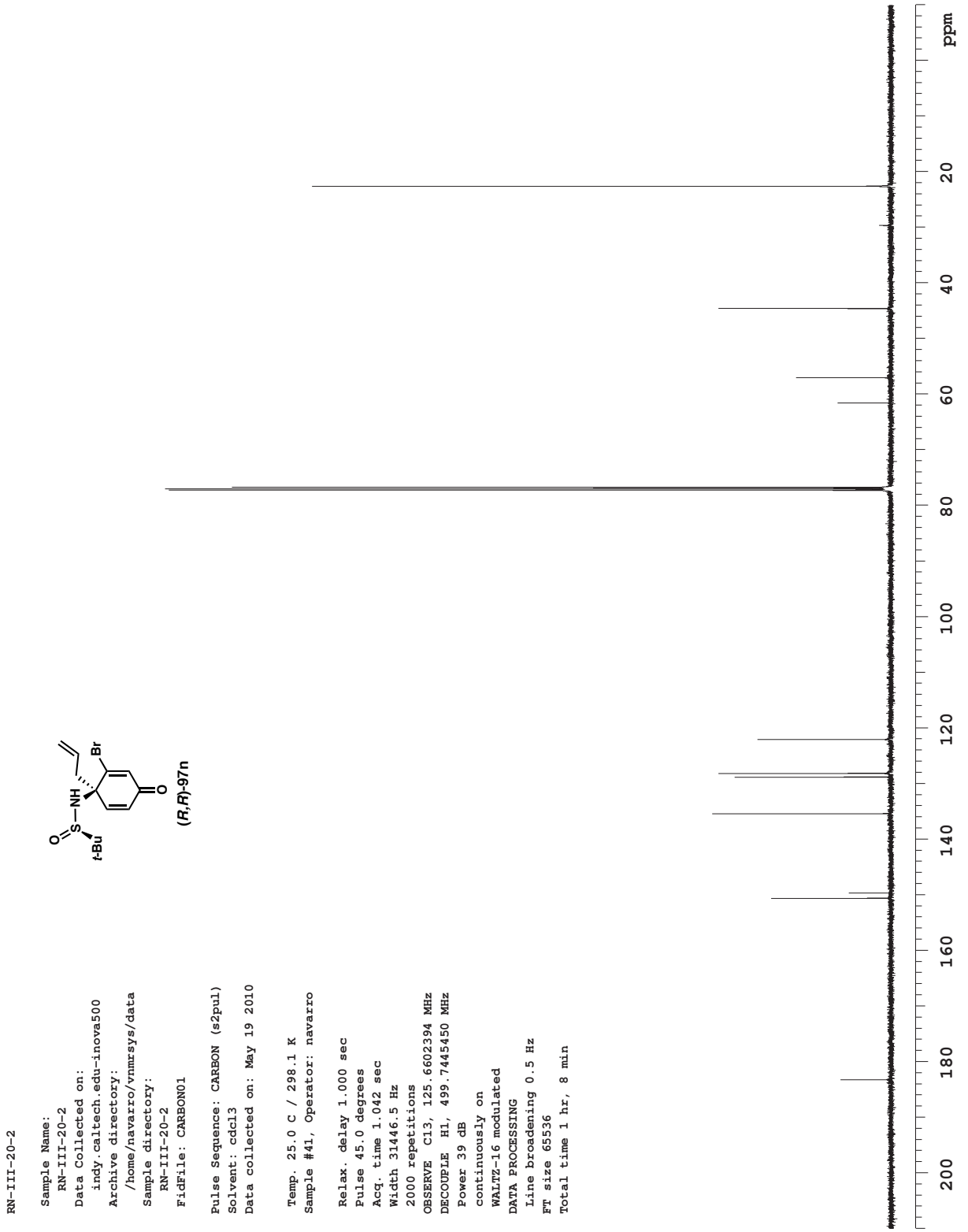

RN-III-60
Sample Name:
RN-III-60
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-60
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 25 2010
Temp. 25.0 C / 298.1 K
Sample #42, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 32768
Total time 1 min 5 sec
Ph
Br
NH
S
O
O
t-Bu
971
ppm
10.41
1.08
1.05
1.00
1.07
0.89
2.16
3.21
1.51

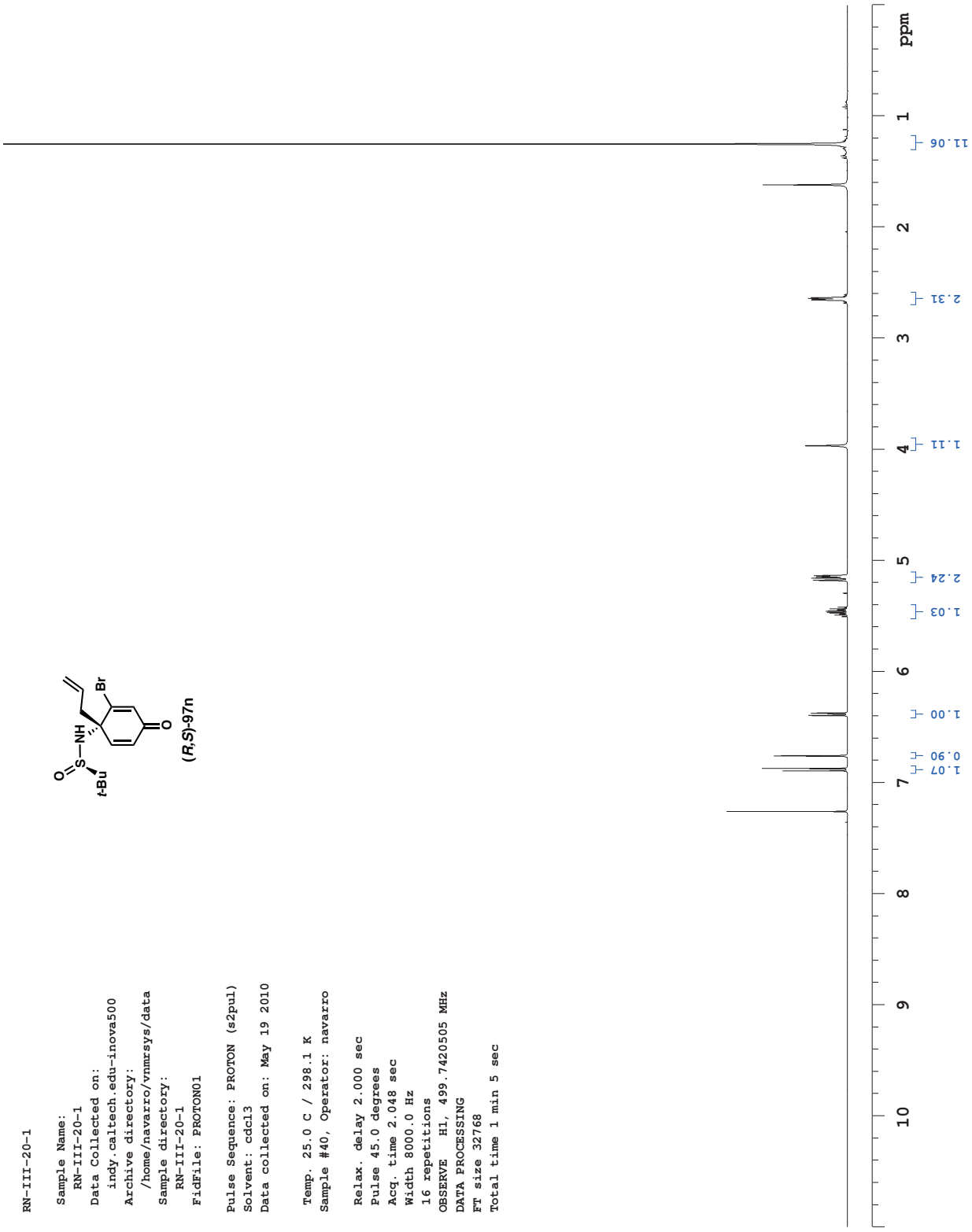

RN-III-60
Sample Name:
RN-III-60
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-60
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 25 2010
Temp. 25.0 C / 298.1 K
Sample #42, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2500 repetitions
OBSERVE C13, 125.6602404 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 25 min
Ph
Br
NH
O
S
O
t-Bu
O
97l
200
180
160
140
120
100
80
60
40
20
ppm


RN-III-75
Sample Name:
RN-III-75
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-75
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 26 2010
Temp. 25.0 C / 298.1 K
Sample #42, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 32768
Total time 1 min 5 sec
97m
ppm
10.43
1.06
2.05
0.99
1.00
0.87
1.07


RN-III-75
Sample Name:
RN-III-75
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-75
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 26 2010
Temp. 25.0 C / 298.1 K
Sample #42, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1700 repetitions
OBSERVE C13, 125.6602404 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 58 min
O
S
NH
t-Bu
Br
O
97m
200
180
160
140
120
100
80
60
40
20
ppm


RN-III-20-2
Sample Name:
RN-III-20-2
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-20-2
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 19 2010
Temp. 25.0 C / 298.1 K
Sample #41, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 32768
Total time 1 min 5 sec
Br
NH
S
O
O
t-Bu
O
(R,R)-97n
ppm
1
2
3
4
5
6
7
8
9
10
11.11
1.17
1.15
1.11
1.21
1.01
1.05
1.00
0.94
1.10


RN-III-20-2
Sample Name:
RN-III-20-2
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-20-2
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 19 2010
Temp. 25.0 C / 298.1 K
Sample #41, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2000 repetitions
OBSERVE C13, 125.6602394 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 8 min
Br
NH
S
O
O
t-Bu
O
(R,R)-97n
200
180
160
140
120
100
80
60
40
20
ppm


RN-III-20-1
Sample Name:
RN-III-20-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-20-1
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 19 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 32768
Total time 1 min 5 sec
t-Bu
S
NH
Br
O
O
(R,S)-97n
ppm
11.06
2.31
1.11
2.24
1.03
1.00
0.90
1.07

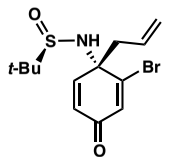
RN-III-20-1

Sample Name:
RN-III-20-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-20-1
FidFile: CARBON01

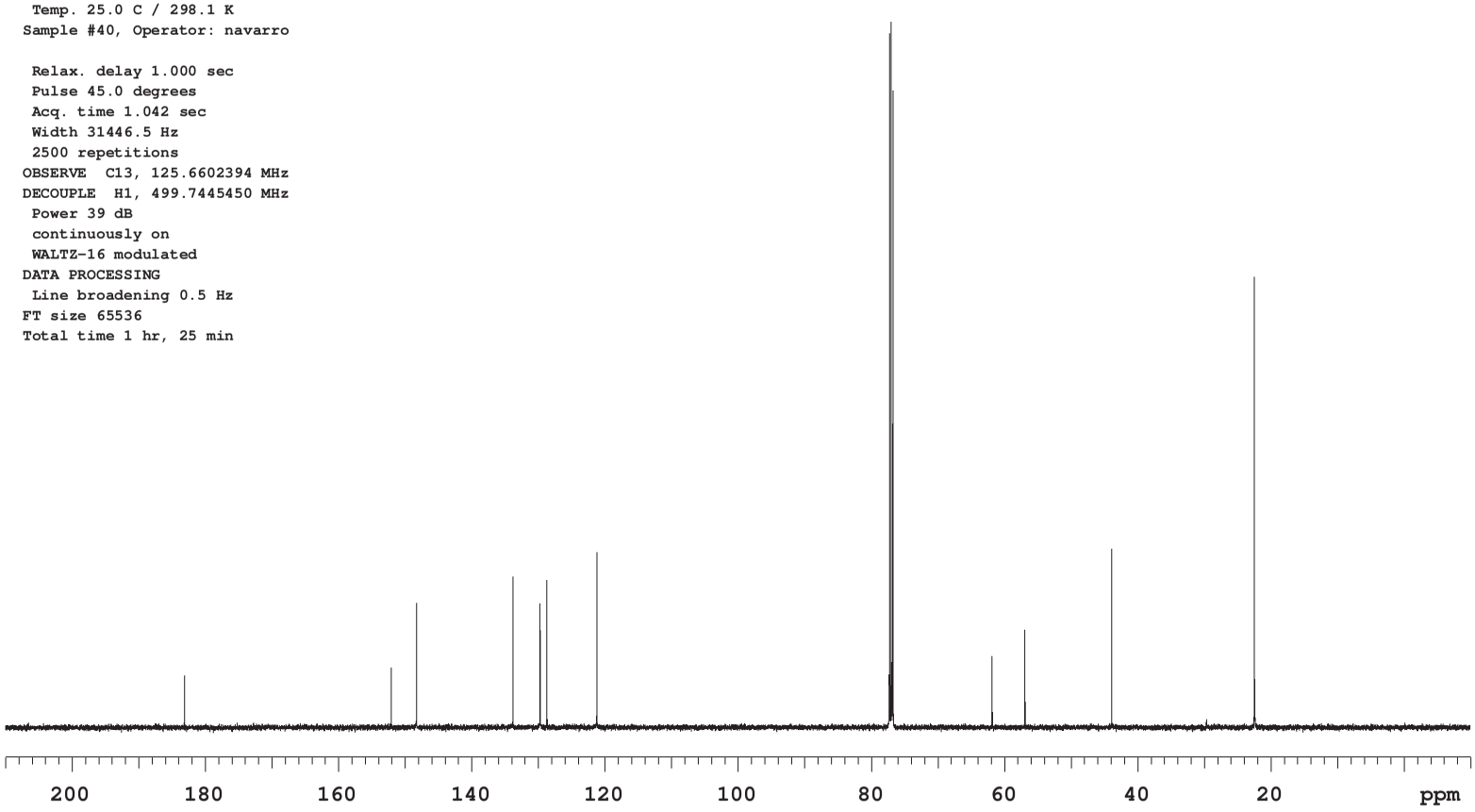
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 19 2010

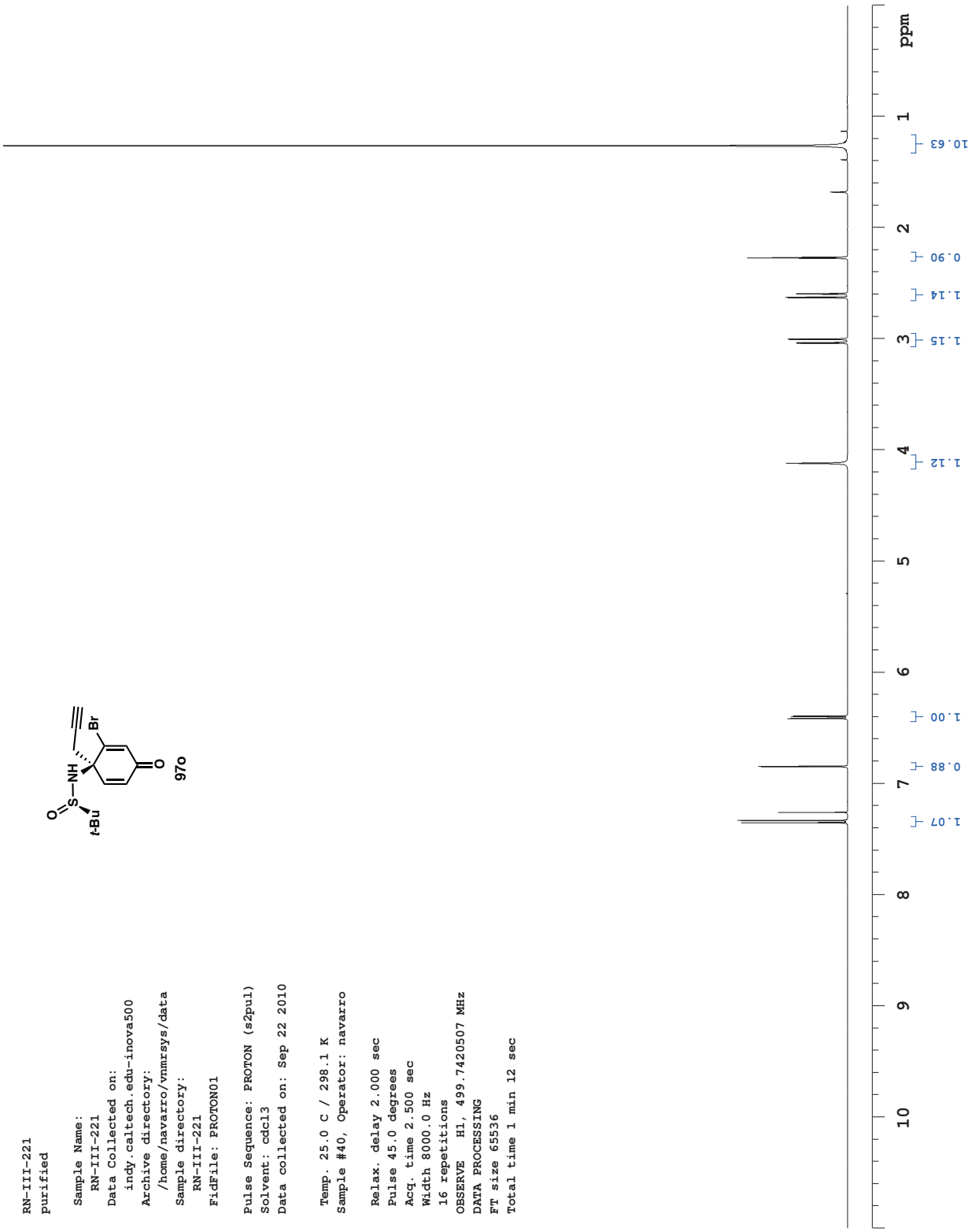
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro

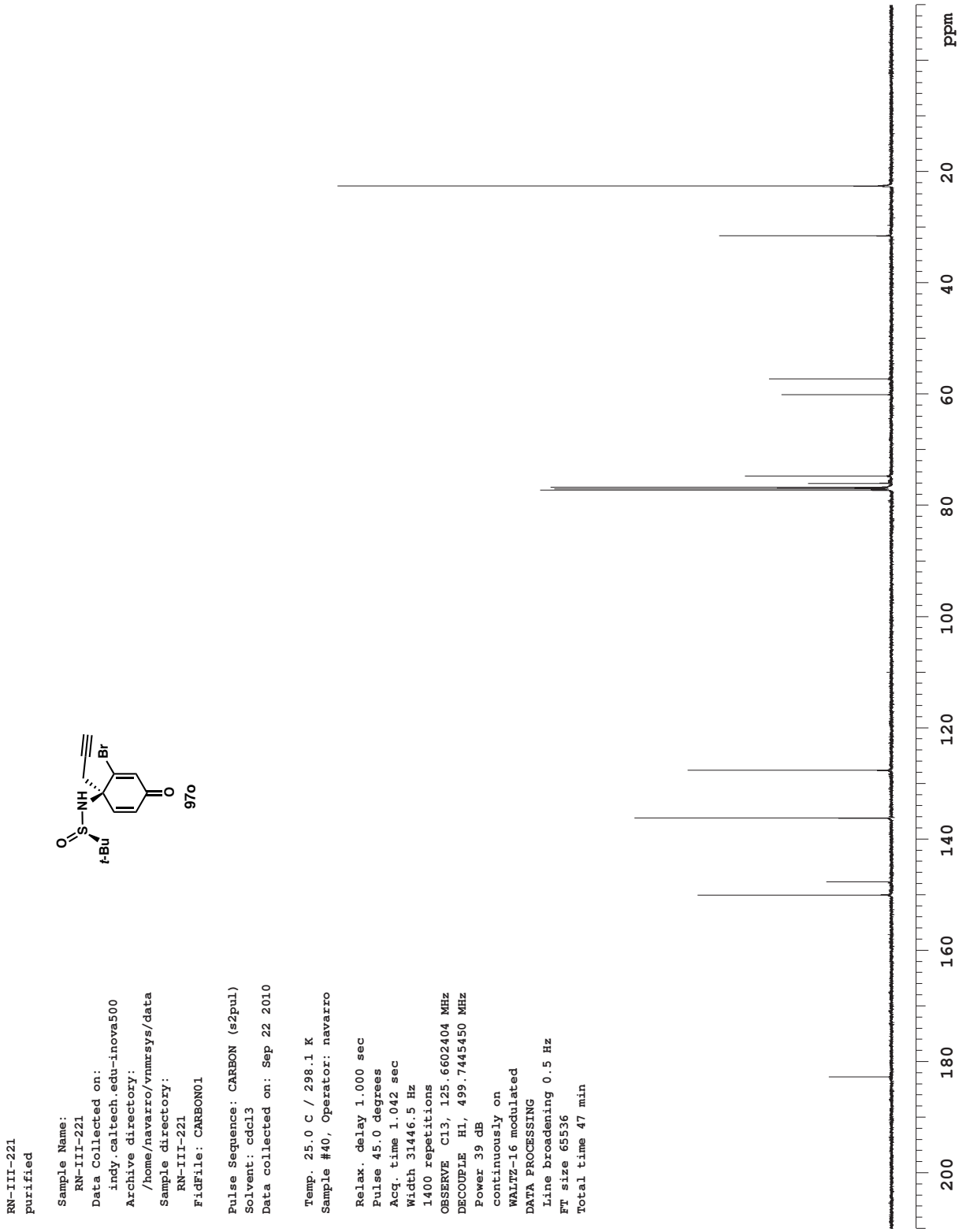
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2500 repetitions
OBSERVE C13, 125.6602394 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 25 min

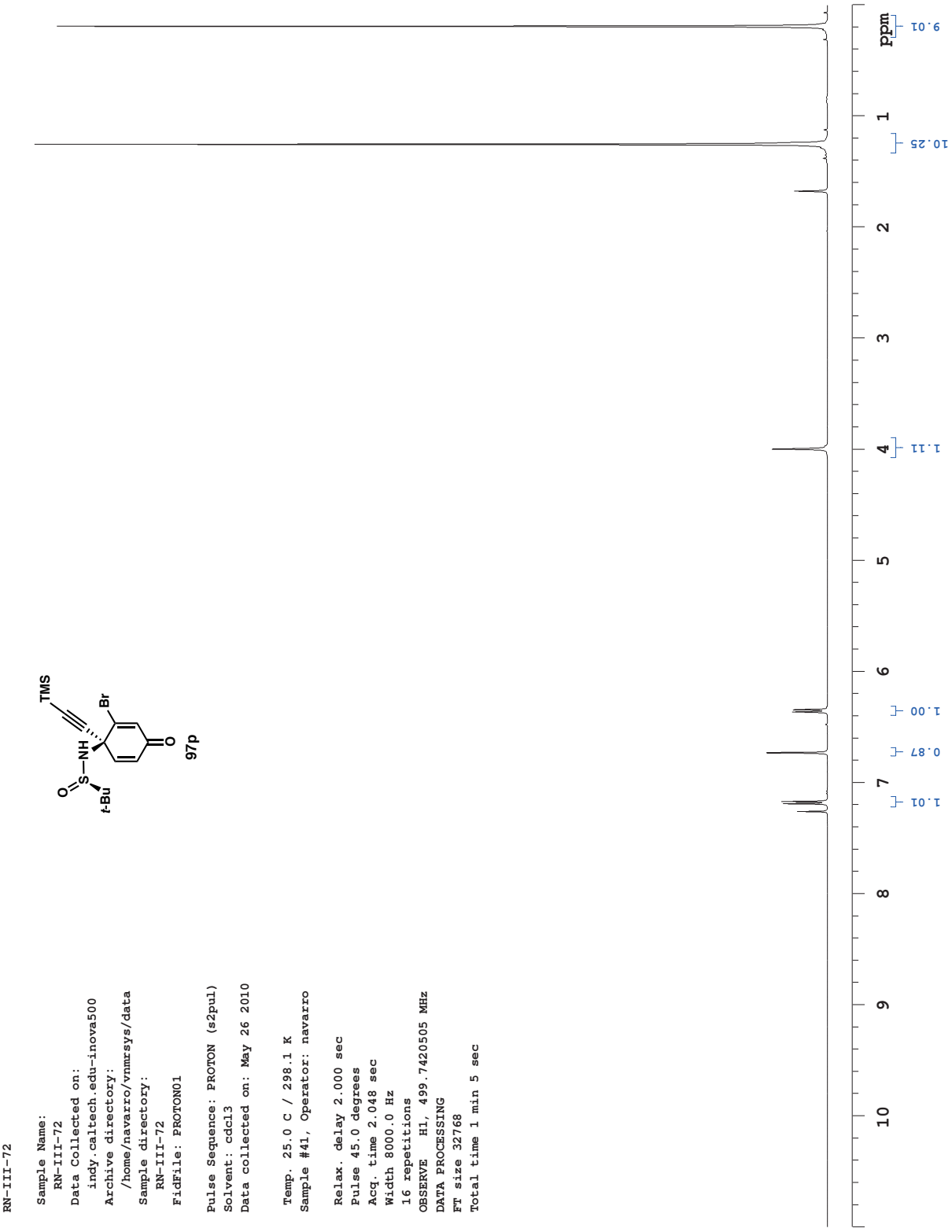


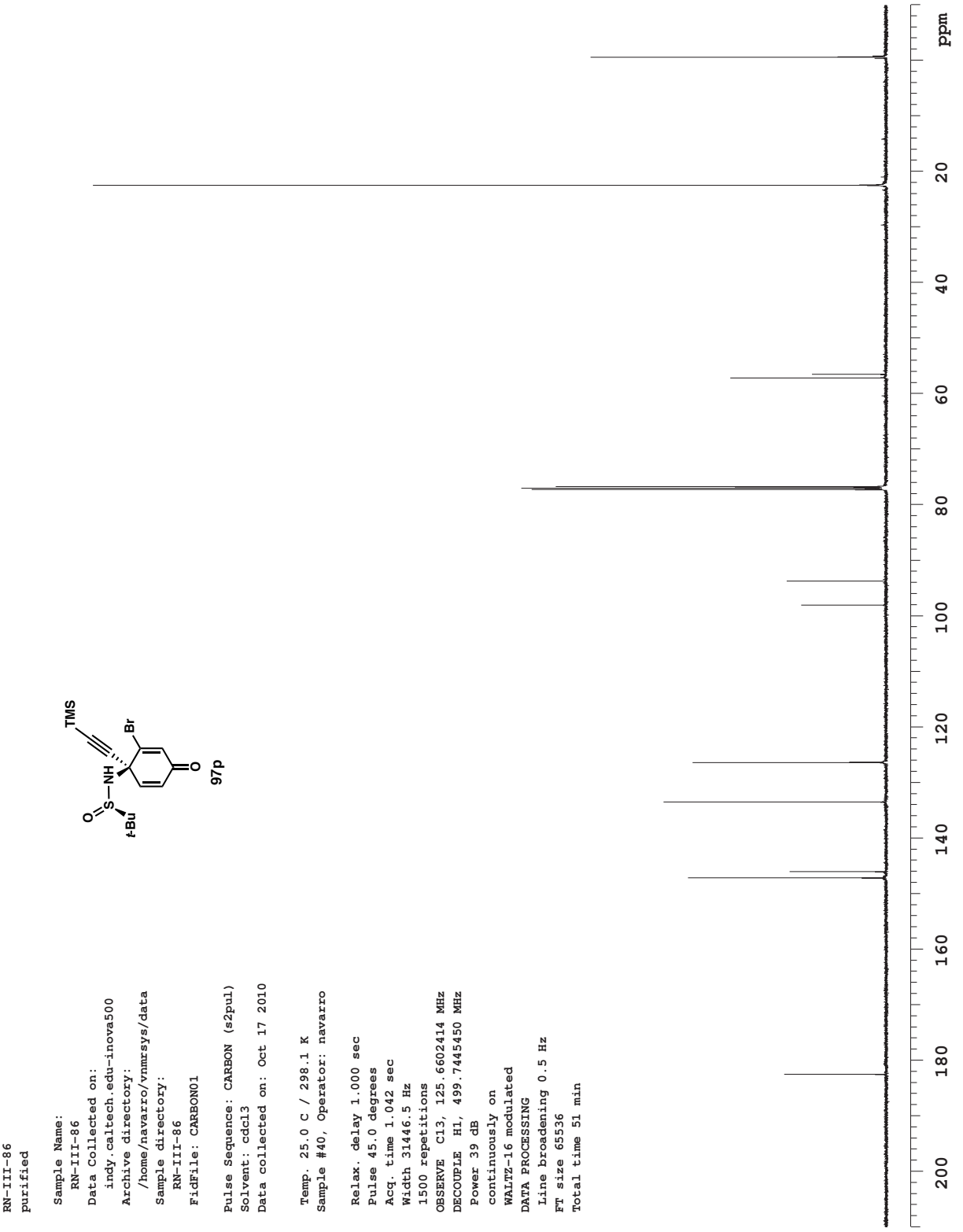
(*R*,*S*)-97n

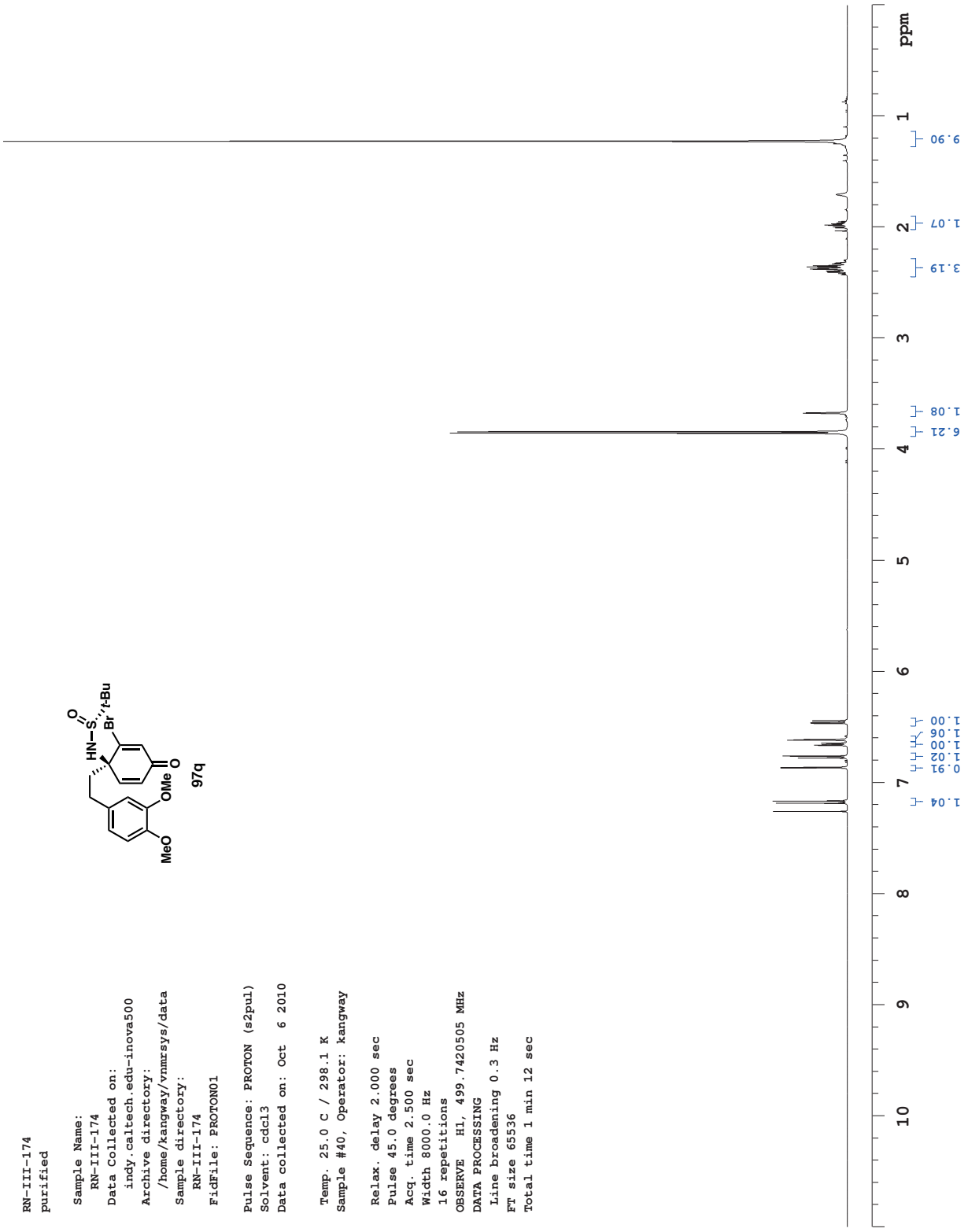



RN-III-221
purified
Sample Name:
RN-III-221
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-221
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 22 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420507 MHz
DATA PROCESSING
FT size 65536
Total time 1 min 12 sec
Br
NH
S
O
O
t-Bu
O
97o
ppm
1
2
3
4
5
6
7
8
9
10
10.63
0.90
1.14
1.15
1.12
1.00
0.88
1.07


RN-III-221
purified
Sample Name:
RN-III-221
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-221
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 22 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1400 repetitions
OBSERVE C13, 125.6602404 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 47 min
Br
NH
S
O
O
t-Bu
O
97o
200
180
160
140
120
100
80
60
40
20
ppm


RN-III-72
Sample Name:
RN-III-72
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-72
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 26 2010
Temp. 25.0 C / 298.1 K
Sample #41, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 32768
Total time 1 min 5 sec
TMS
Br
NH
S
O
O
t-Bu
O
97p
ppm
10
9
8
7
6
5
4
3
2
1
9.01
10.25
1.11
1.00
0.87
1.01


RN-III-86
purified
Sample Name:
RN-III-86
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-86
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 17 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6602414 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
TMS
Br
NH
S
O
O
t-Bu
O
97p
200
180
160
140
120
100
80
60
40
20
ppm


RN-III-174
purified
Sample Name:
RN-III-174
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
RN-III-174
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 6 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: kangway
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
Line broadening 0.3 Hz
FT size 65536
Total time 1 min 12 sec
HN
S
O
Br
t-Bu
OMe
O
MeO
97q
ppm
10
9
8
7
6
5
4
3
2
1
9.90
1.07
3.19
1.08
6.21
1.04
0.91
1.02
1.00
1.06
1.00
1.00

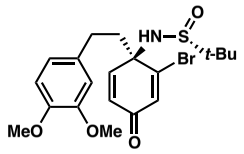
RN-III-174
purified

Sample Name:
RN-III-174
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
RN-III-174
FidFile: CARBON01

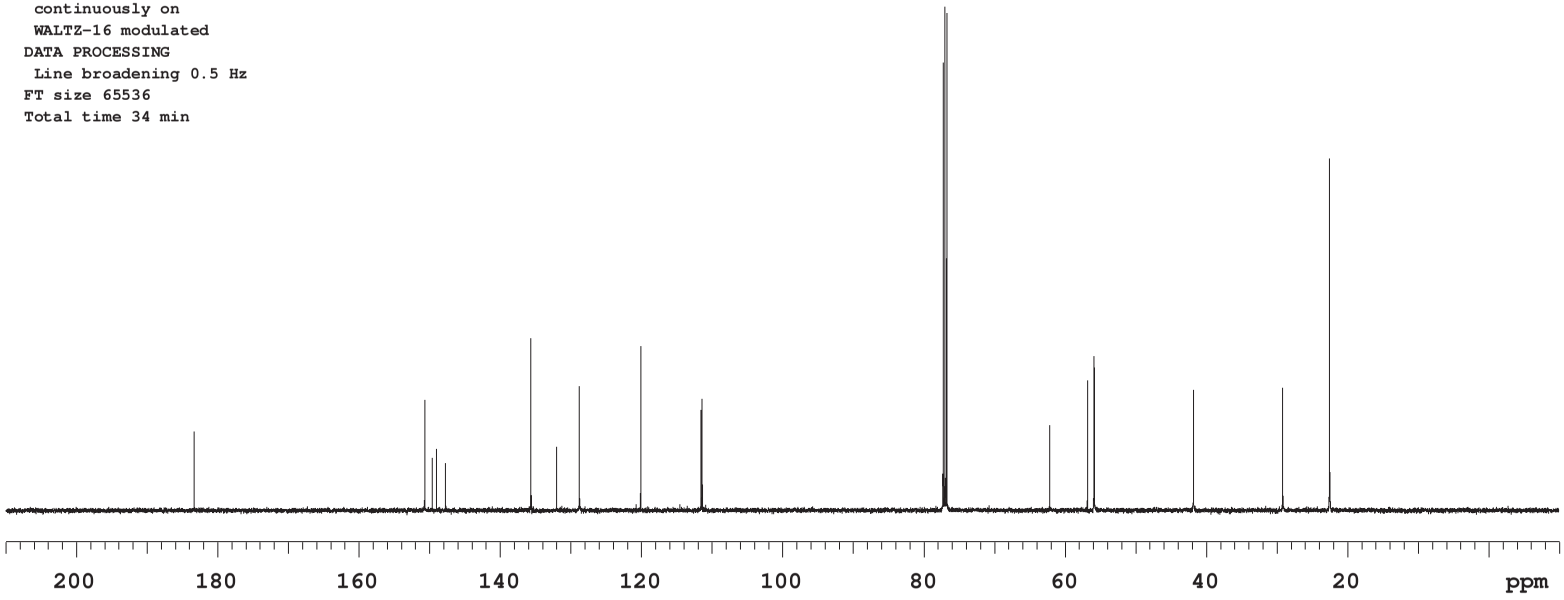
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 6 2010

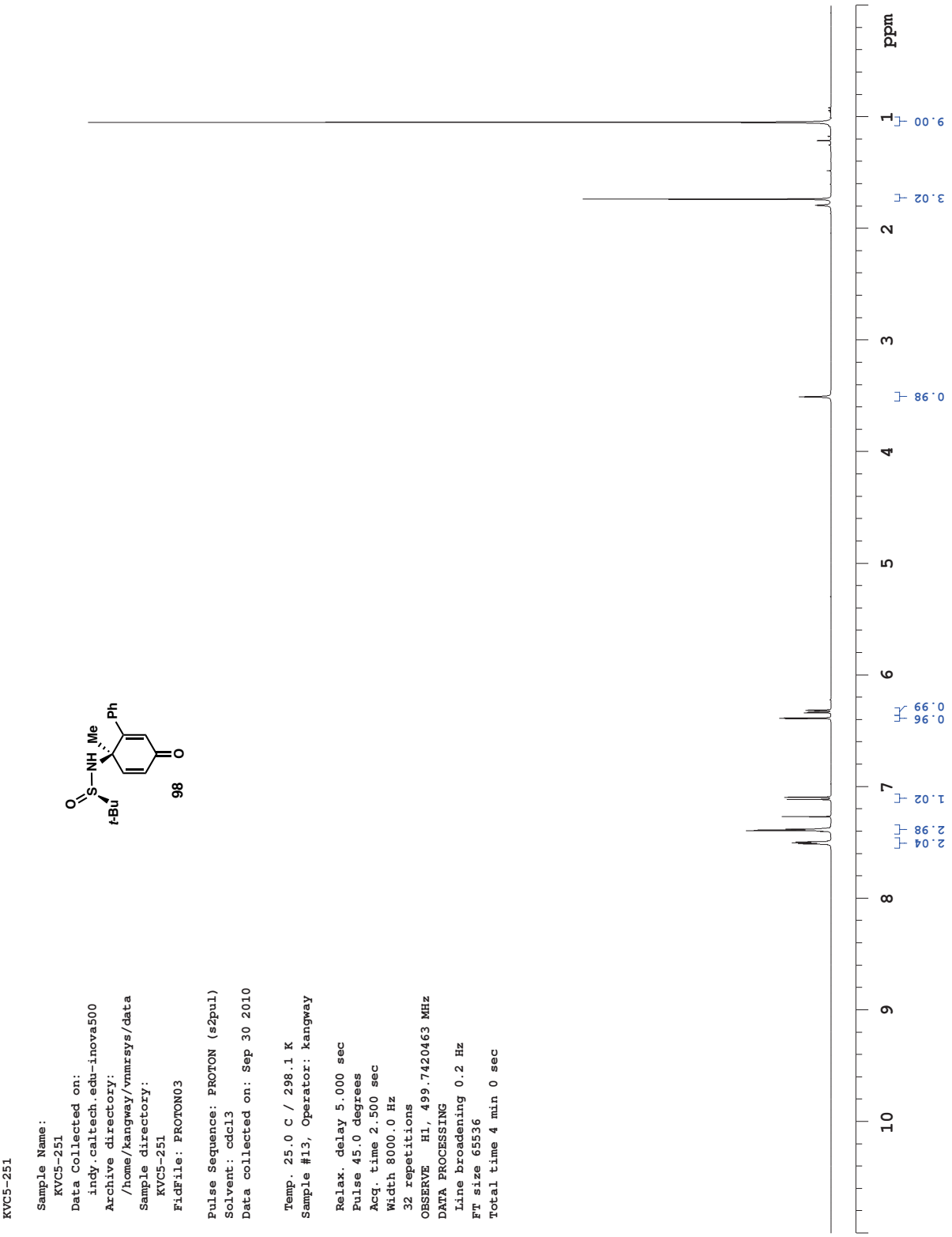
Temp. 25.0 C / 298.1 K
Sample #40, Operator: kangway

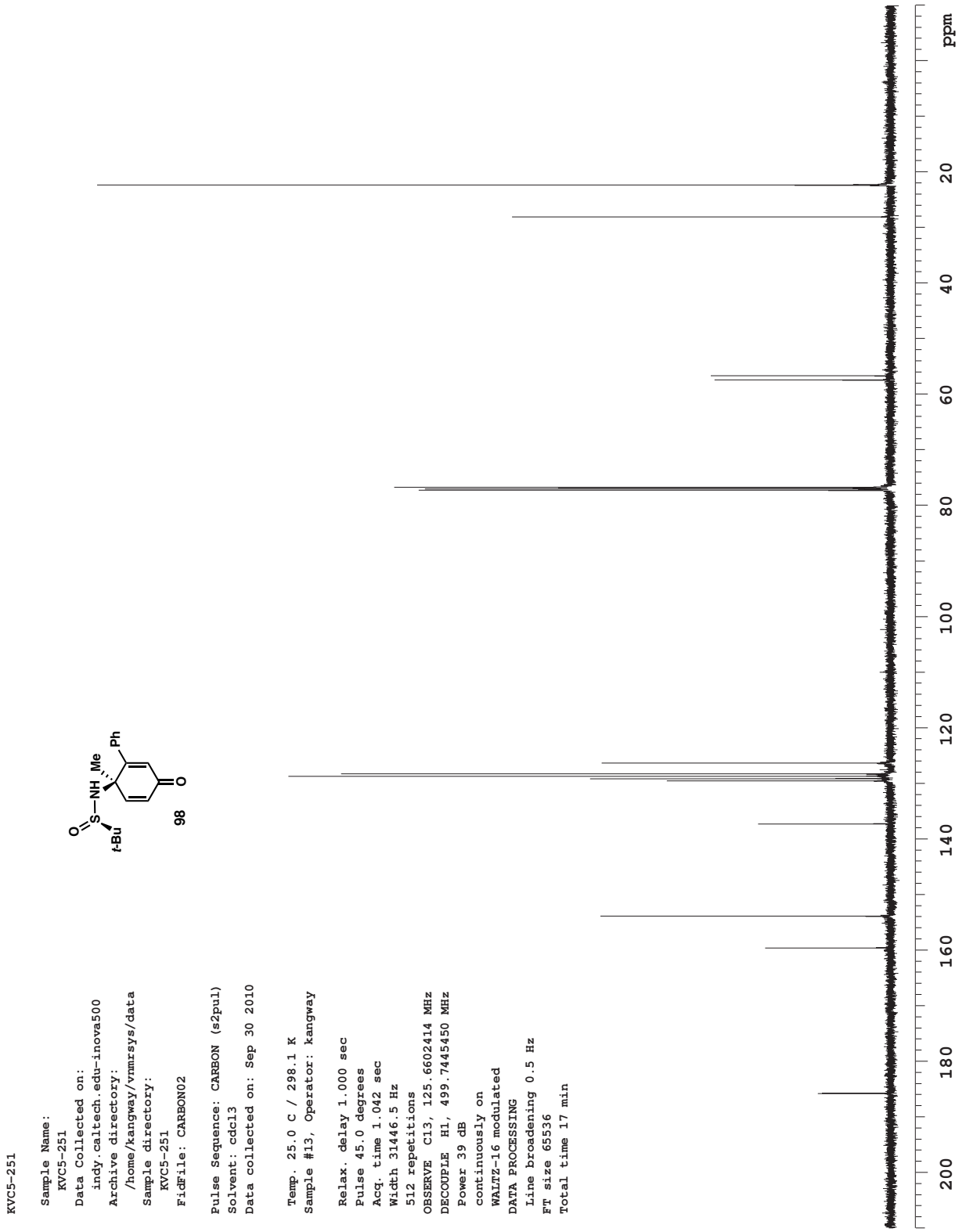
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6602414 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min

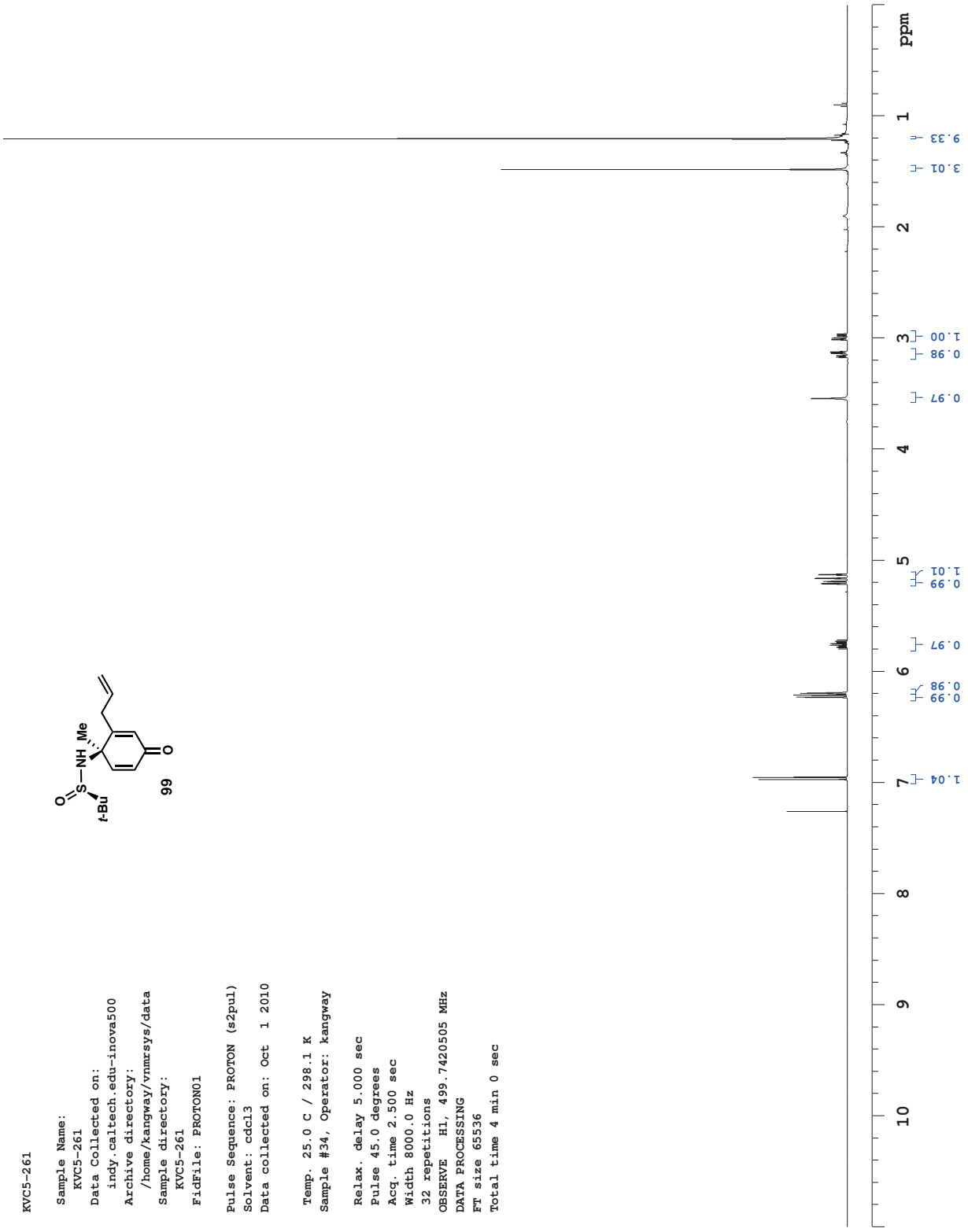


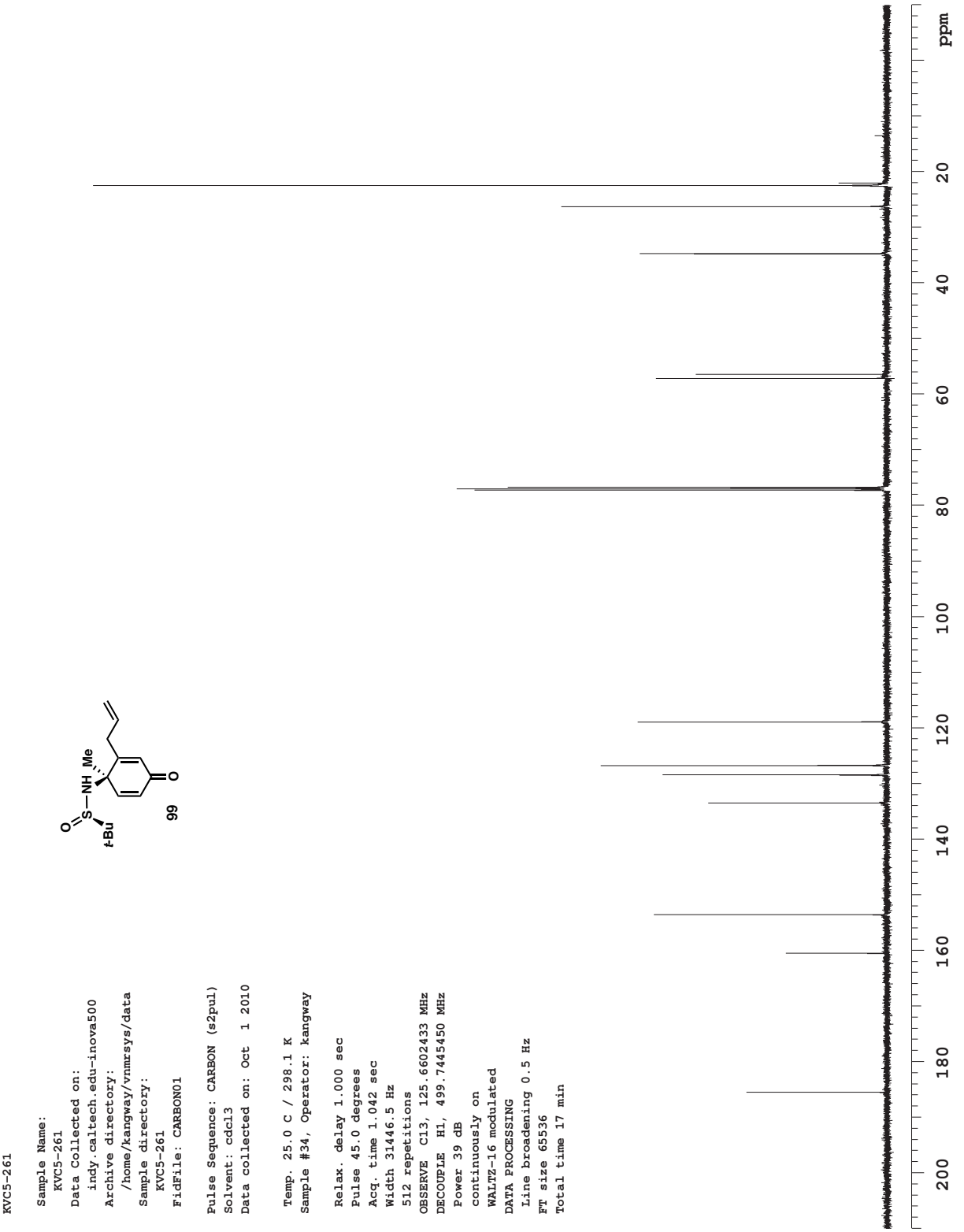
97q

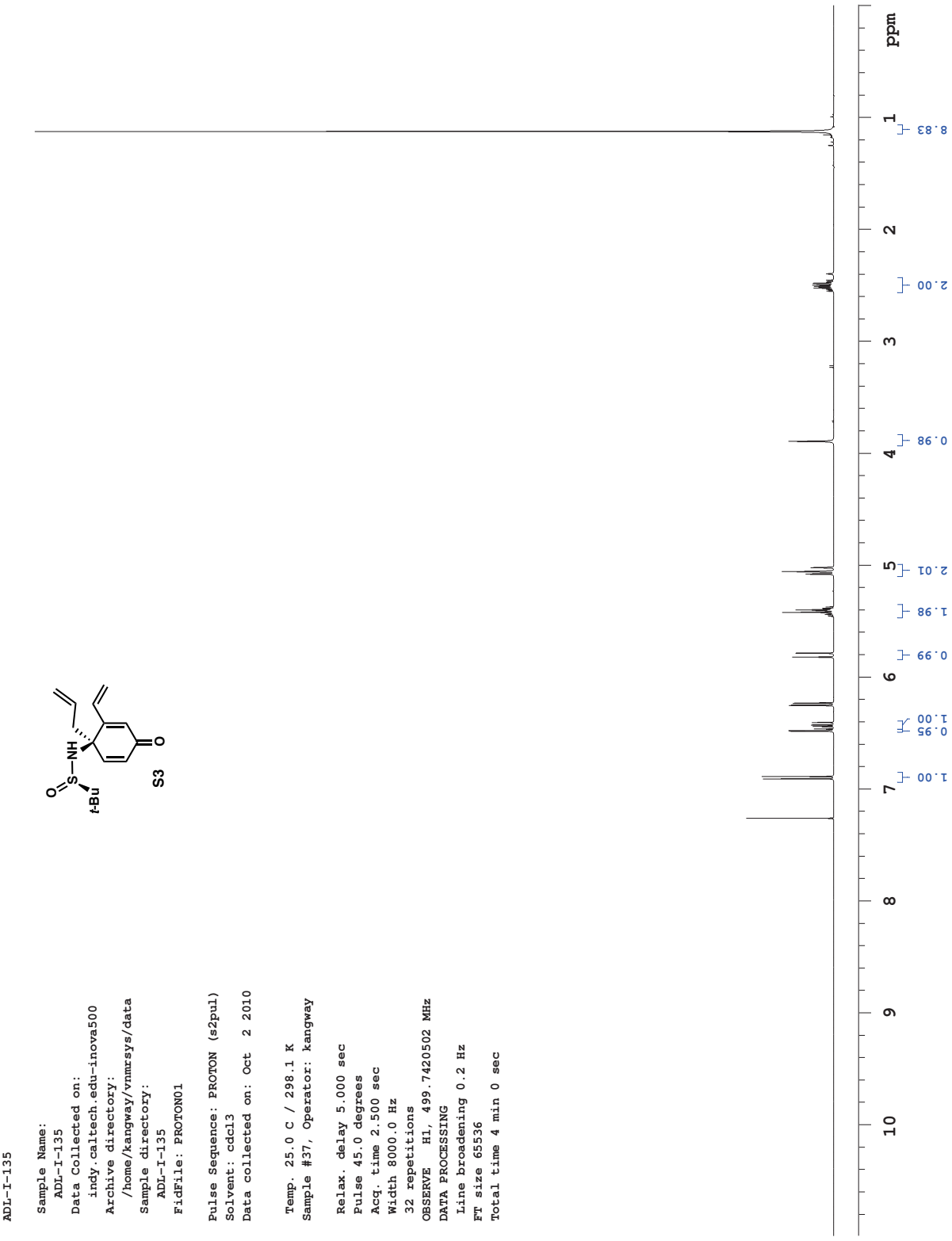


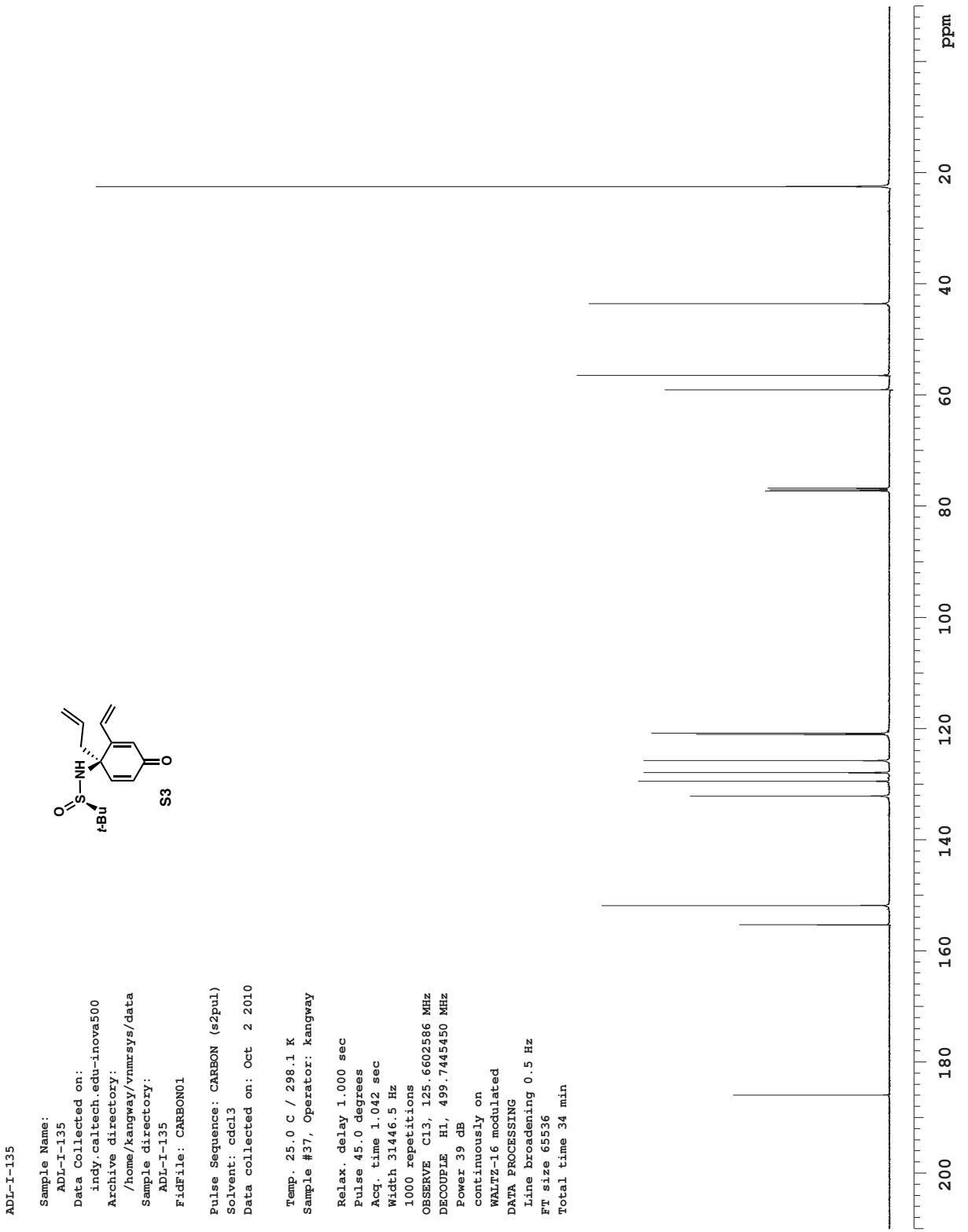

KVC5-251
Sample Name:
KVC5-251
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC5-251
FidFile: PROTON03
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 30 2010
Temp. 25.0 C / 298.1 K
Sample #13, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7420463 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
O
S
NH
Me
Ph
t-Bu
O
98
ppm
10
9
8
7
6
5
4
3
2
1
9.00
3.02
0.98
0.99
0.96
1.02
2.98
2.04


KVC5-251
Sample Name:
KVC5-251
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC5-251
FidFile: CARBON02
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 30 2010
Temp. 25.0 C / 298.1 K
Sample #13, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6602414 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
O
S
NH
Me
Ph
t-Bu
O
98
200
180
160
140
120
100
80
60
40
20
ppm

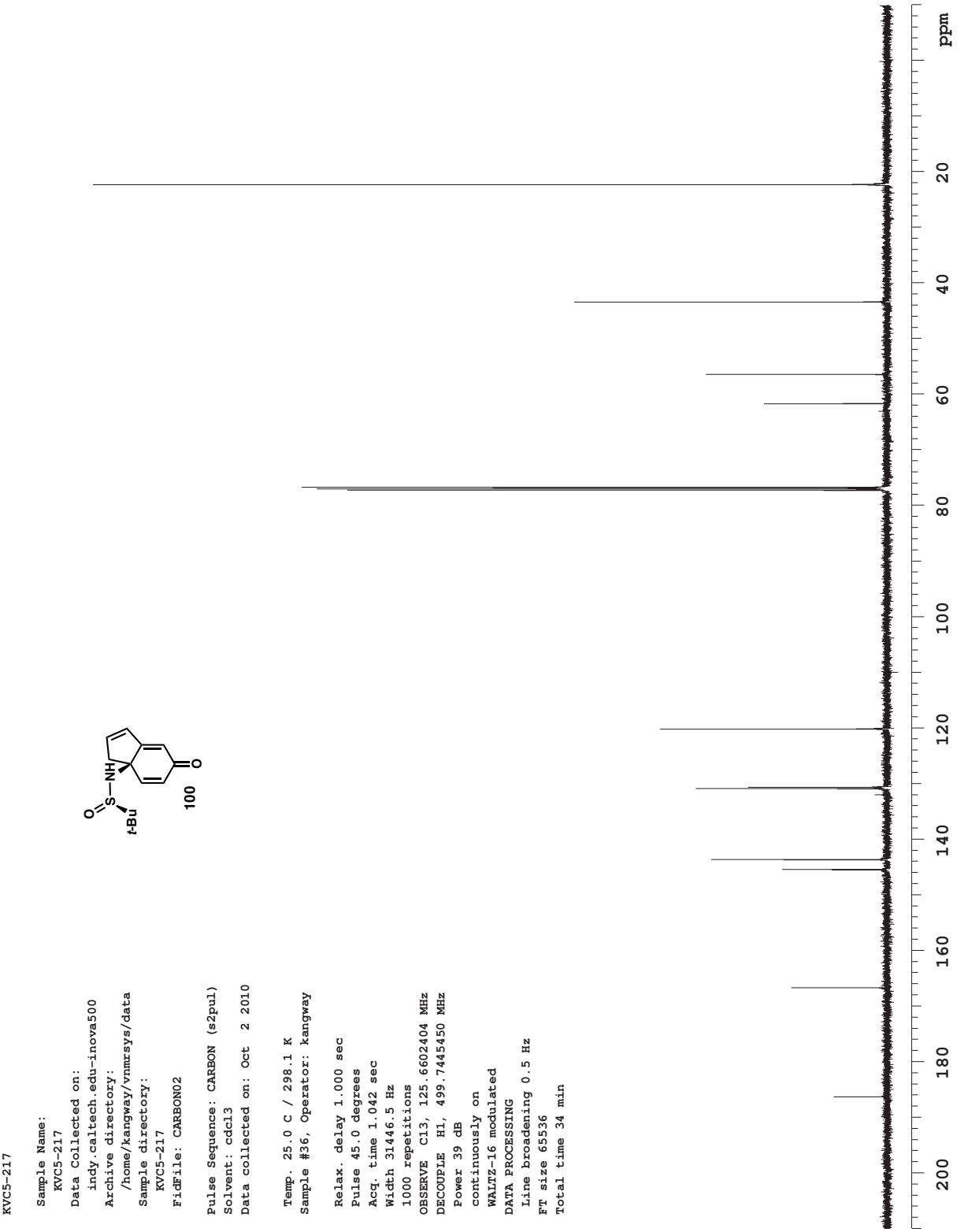

KVC5-261
Sample Name:
KVC5-261
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC5-261
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 1 2010
Temp. 25.0 C / 298.1 K
Sample #34, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 65536
Total time 4 min 0 sec
99
ppm
9.33
3.01
1.00
0.98
0.97
1.01
0.99
0.97
0.98
0.99
1.04

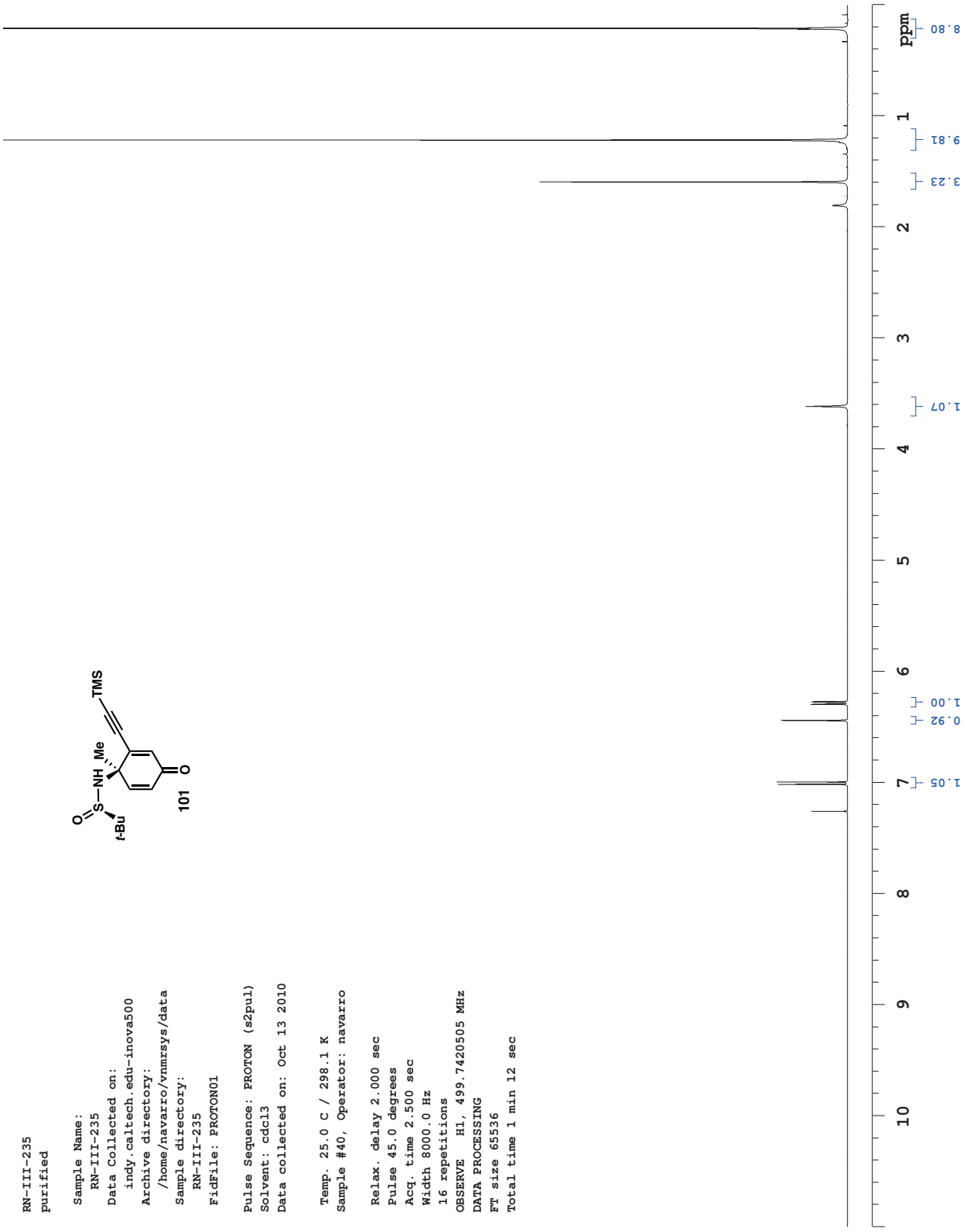

KVC5-261
Sample Name:
KVC5-261
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC5-261
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 1 2010
Temp. 25.0 C / 298.1 K
Sample #34, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6602433 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
O
S
NH
Me
t-Bu
O
99
200
180
160
140
120
100
80
60
40
20
ppm


ADL-I-135
Sample Name:
ADL-I-135
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
ADL-I-135
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 2 2010
Temp. 25.0 C / 298.1 K
Sample #37, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7420502 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
S3
t-Bu
NH
ppm
8.83
2.00
0.98
2.01
1.98
0.99
0.95
1.00
1.00


ADL-I-135
Sample Name:
ADL-I-135
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
ADL-I-135
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 2 2010
Temp. 25.0 C / 298.1 K
Sample #37, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6602586 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
S3
t-Bu
200
180
160
140
120
100
80
60
40
20
ppm


KVC5-217
Sample Name:
KVC5-217
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC5-217
FidFile: PROTON03
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 2 2010
Temp. 25.0 C / 298.1 K
Sample #38, Operator: kangway
Relax. delay 10.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 6 min 40 sec
NH
S
O
O
t-Bu
O
100
ppm
1
2
3
4
5
6
7
8
9
10
9.12
1.96
0.95
0.98
1.00
1.02
0.98
1.01


KVC5-217
Sample Name:
KVC5-217
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC5-217
FidFile: CARBON02
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 2 2010
Temp. 25.0 C / 298.1 K
Sample #36, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6602404 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
NH
S
O
O
t-Bu
O
100
200
180
160
140
120
100
80
60
40
20
ppm


RN-III-235
purified
Sample Name:
RN-III-235
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-235
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 13 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 65536
Total time 1 min 12 sec
TMS
Me
NH
S
O
O
t-Bu
101
ppm
8.80
9.81
3.23
1.07
1.00
0.92
1.05

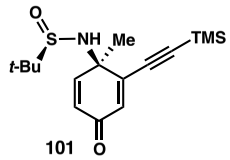
RN-III-235
purified

Sample Name:
RN-III-235
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-235
FidFile: CARBON01

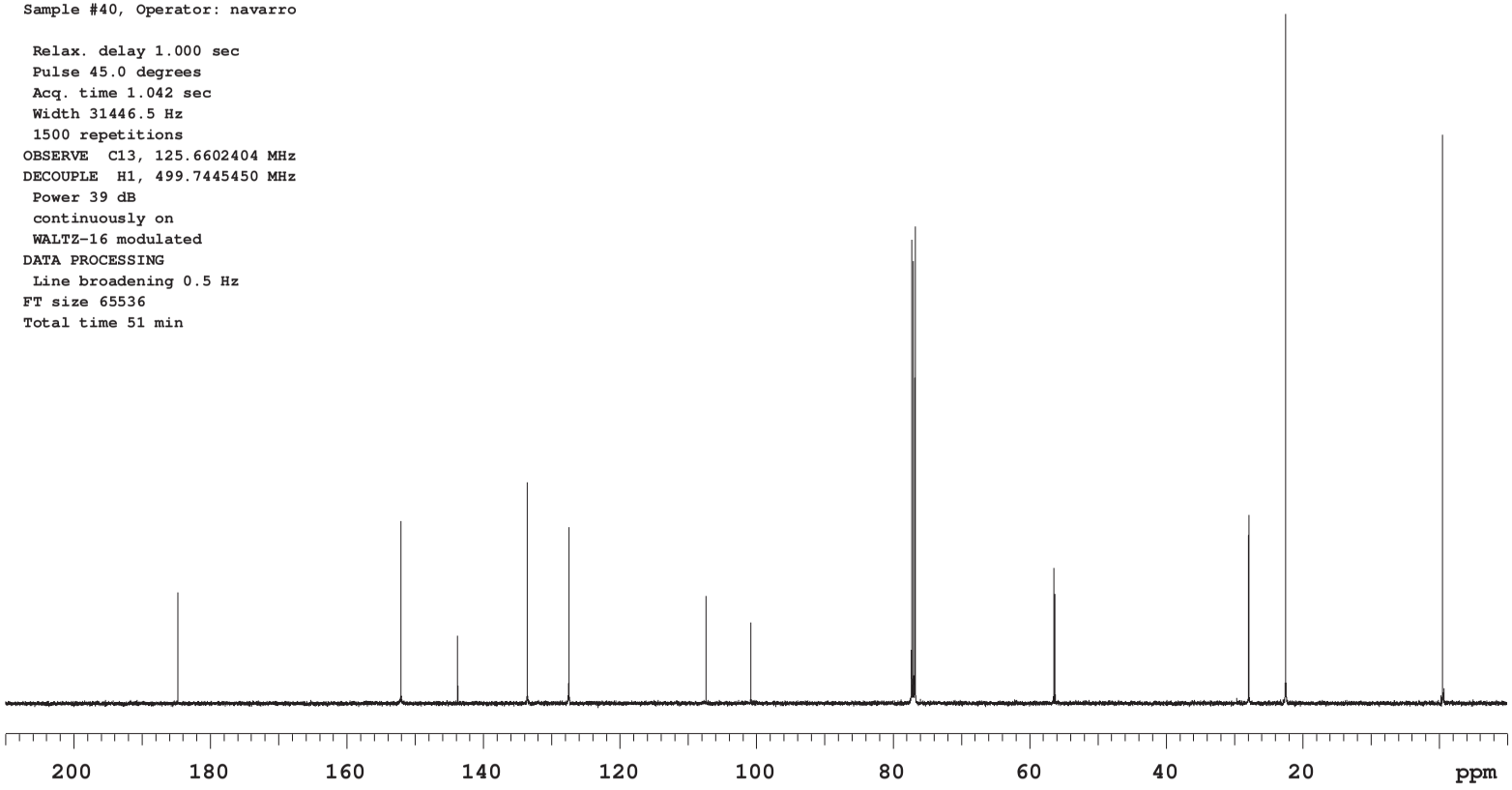
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 13 2010

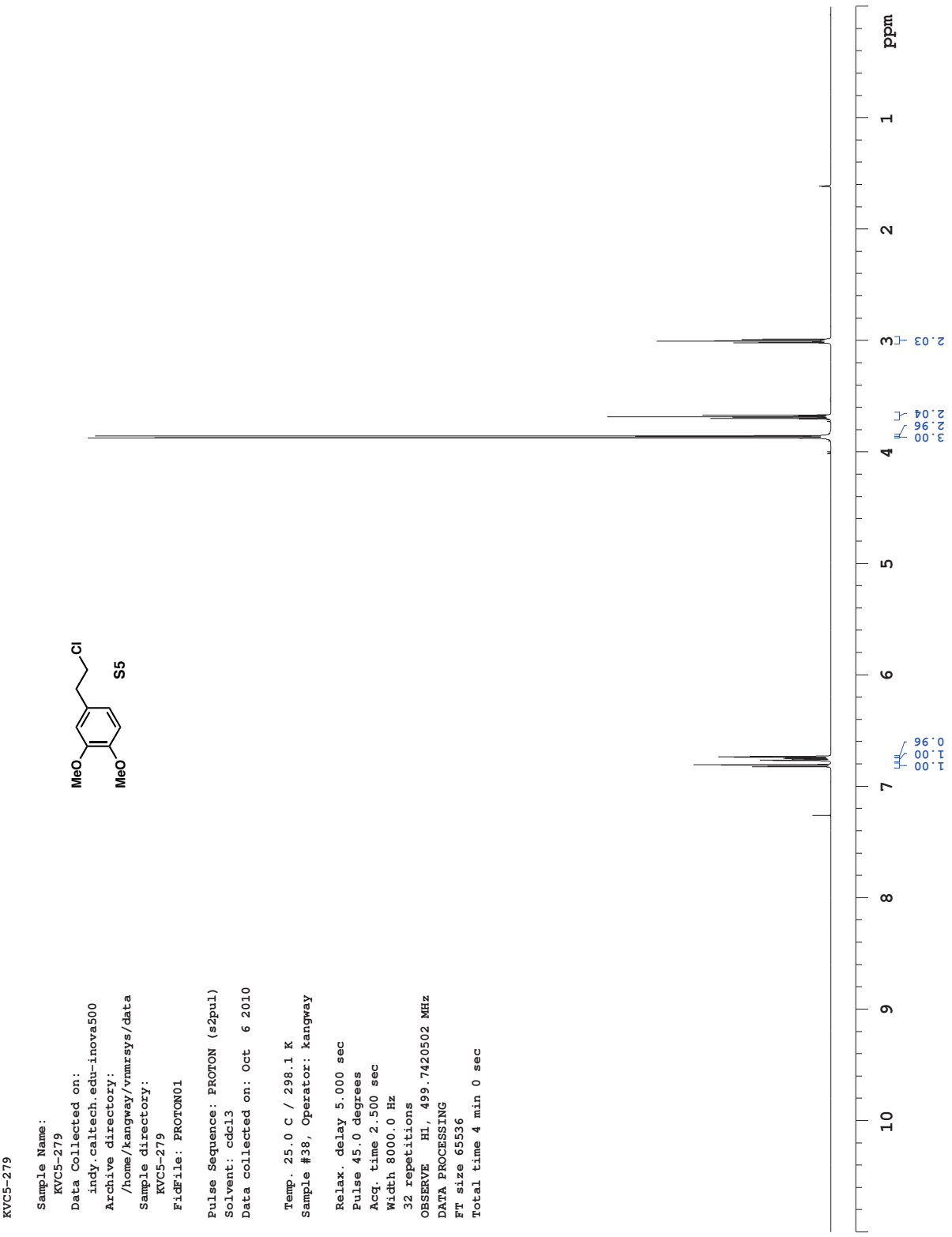
Temp. 25.0 C / 298.1 K
Sample #40, Operator: navarro

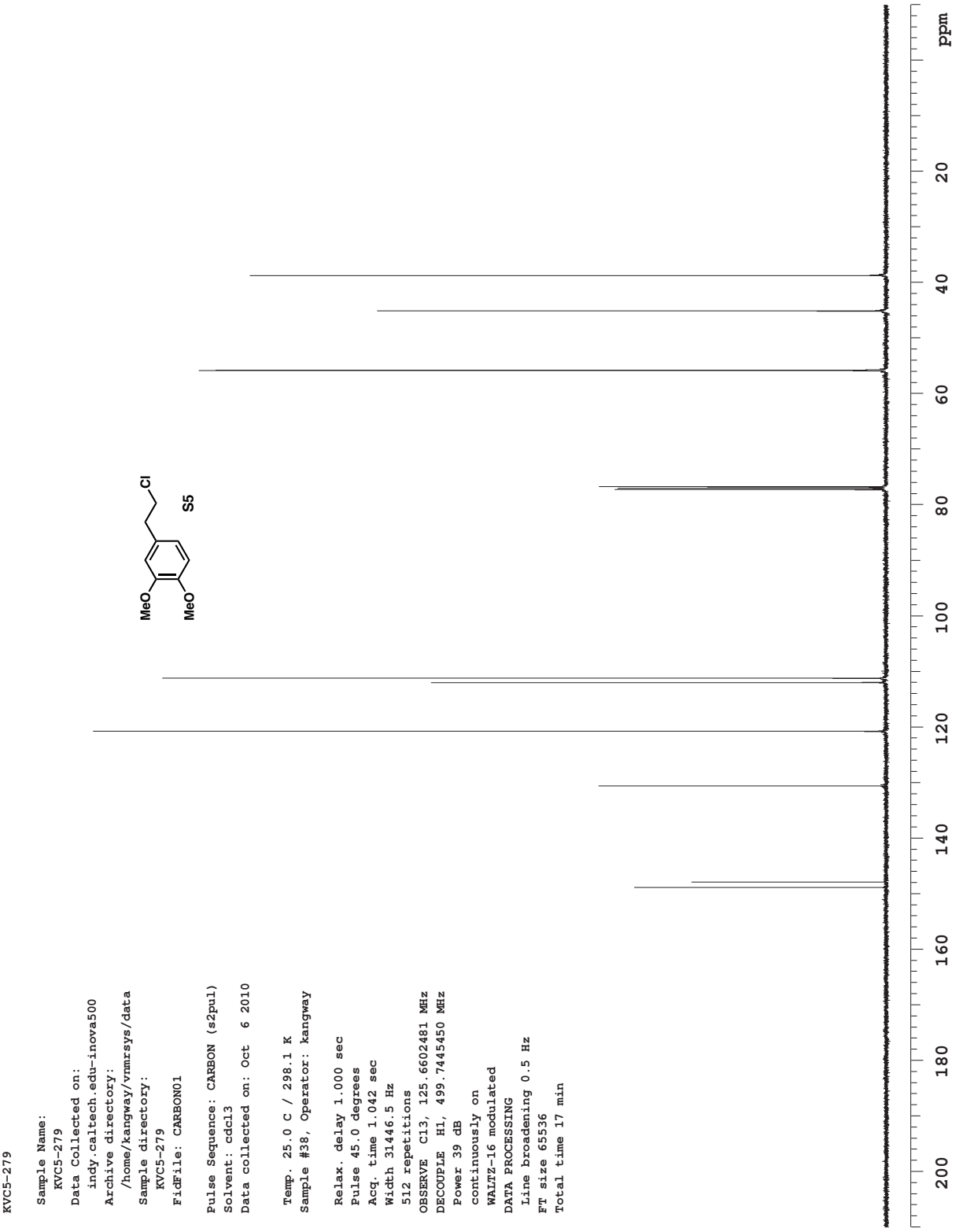
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6602404 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min

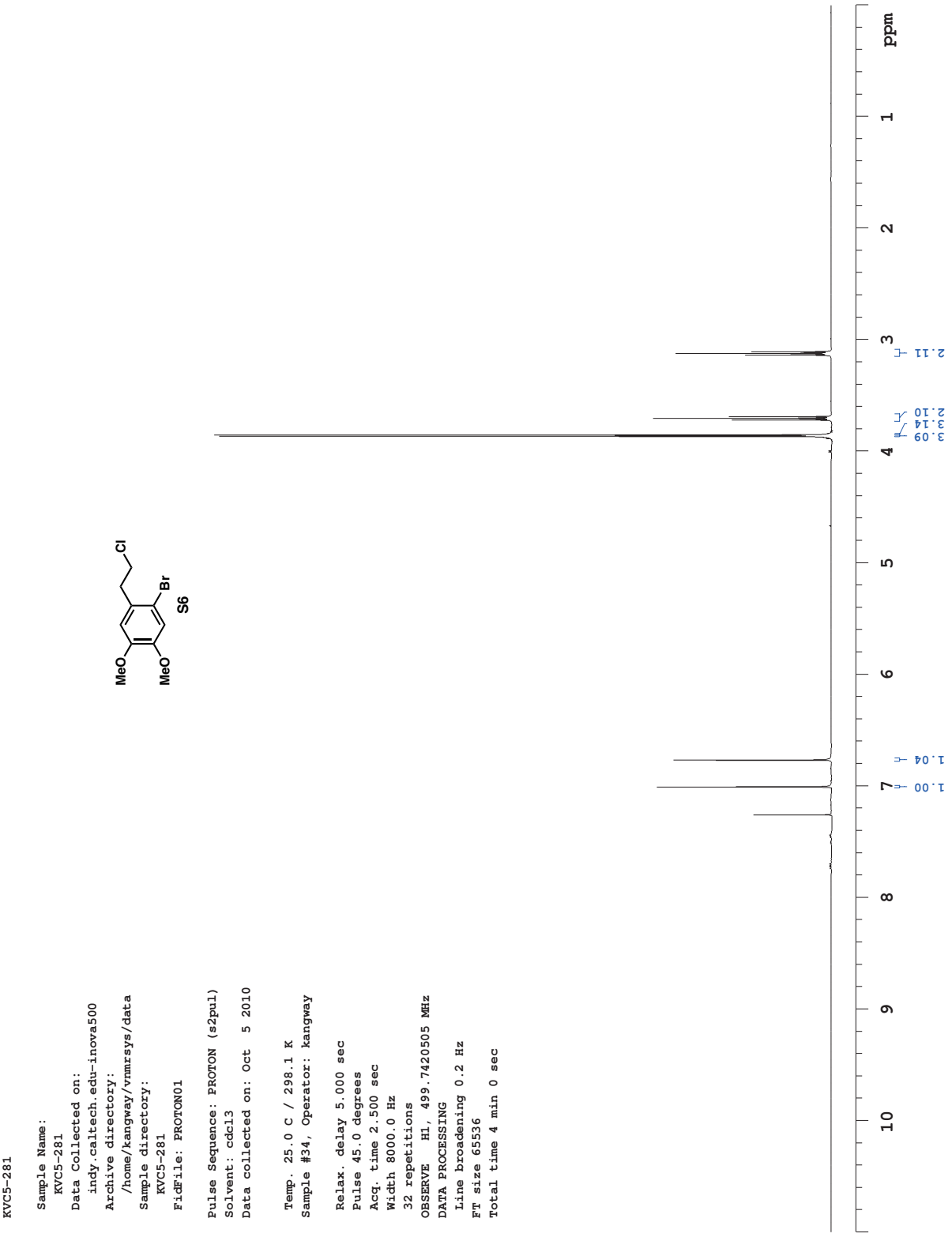


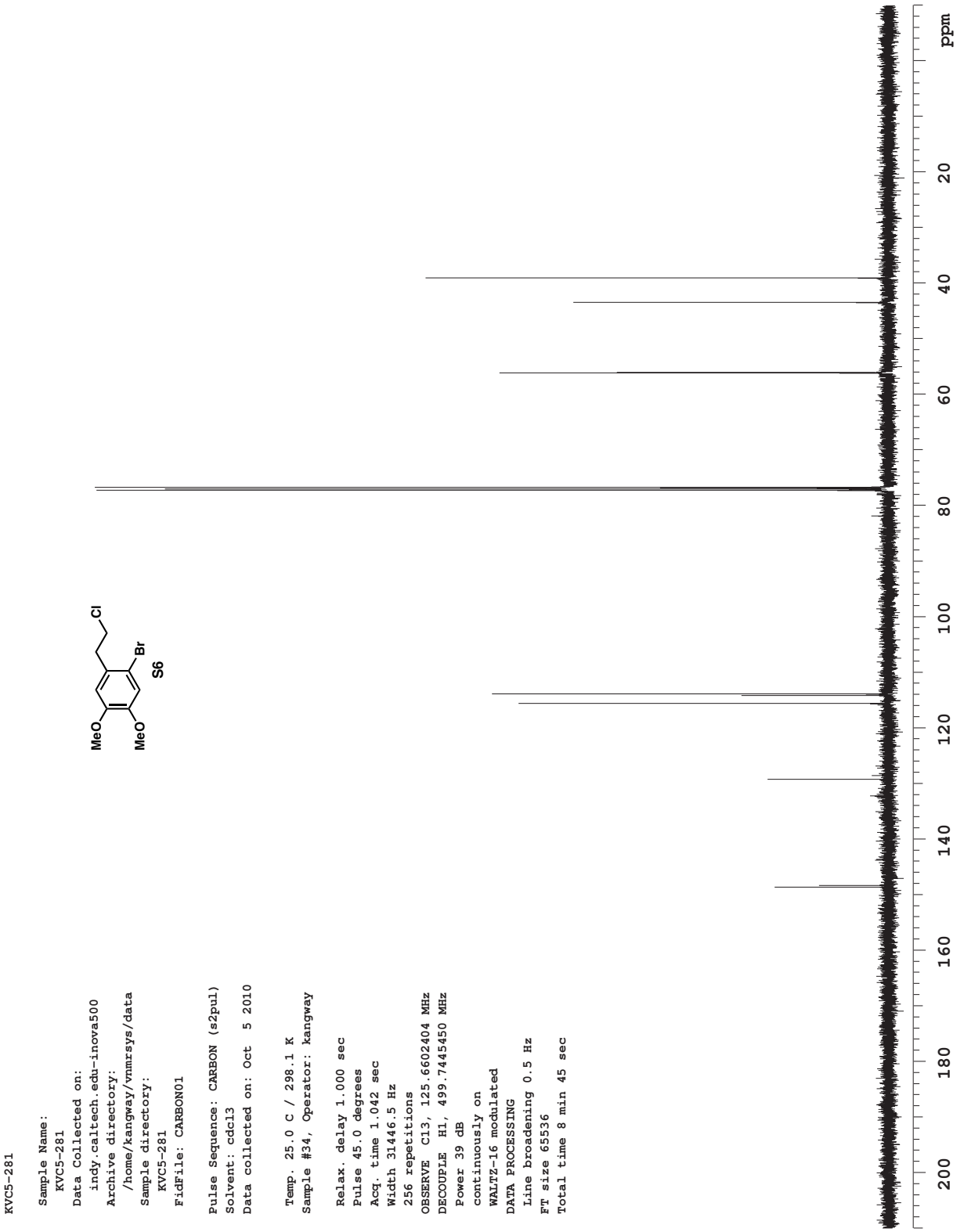
101

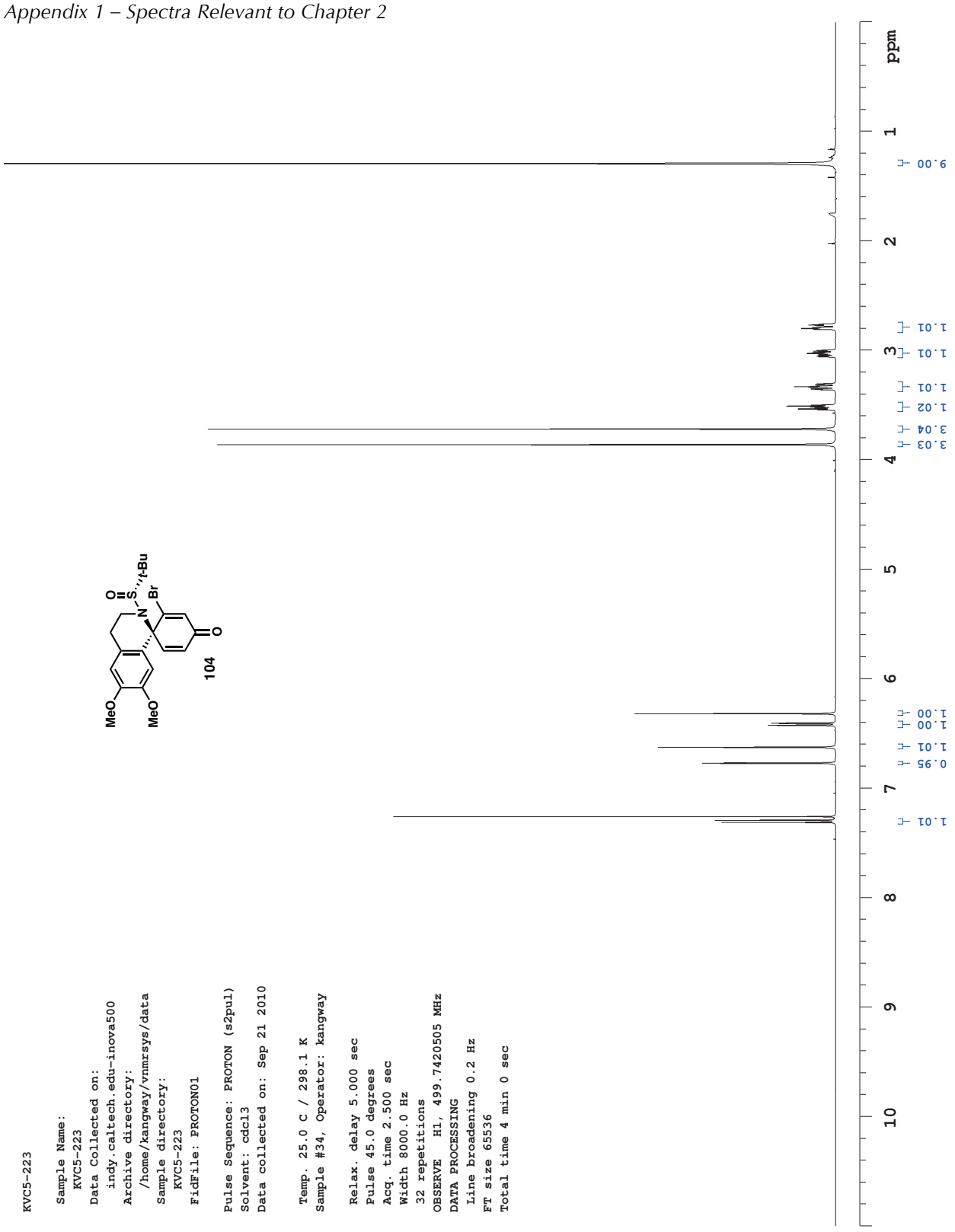



KVC5-279
Sample Name:
KVC5-279
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC5-279
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 6 2010
Temp. 25.0 C / 298.1 K
Sample #38, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7420502 MHz
DATA PROCESSING
FT size 65536
Total time 4 min 0 sec
Cl
MeO
MeO
S5
2.03
3.00
2.96
2.04
1.00
1.00
0.96
ppm


KVC5-279
Sample Name:
KVC5-279
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC5-279
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 6 2010
Temp. 25.0 C / 298.1 K
Sample #38, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6602481 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
MeO
MeO
Cl
S5
200
180
160
140
120
100
80
60
40
20
ppm


KVC5-281
Sample Name:
KVC5-281
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC5-281
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 5 2010
Temp. 25.0 C / 298.1 K
Sample #34, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Cl
Br
MeO
MeO
S6
ppm
1.00
1.04
3.09
3.14
2.10
2.11


KVC5-281
Sample Name:
KVC5-281
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC5-281
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 5 2010
Temp. 25.0 C / 298.1 K
Sample #34, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
256 repetitions
OBSERVE C13, 125.6602404 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 8 min 45 sec
Cl
Br
MeO
MeO
S6
200
180
160
140
120
100
80
60
40
20
ppm


KVC5-223
Sample Name:
KVC5-223
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC5-223
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 21 2010
Temp. 25.0 C / 298.1 K
Sample #34, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
MeO
MeO
Br
t-Bu
104
ppm
9.00
1.01
1.01
1.01
1.02
3.04
3.03
1.00
1.00
1.01
0.95
1.01

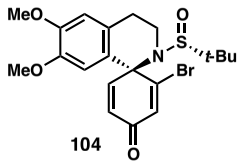
KVC5-223

Sample Name:
KVC5-223
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC5-223
FidFile: CARBON01

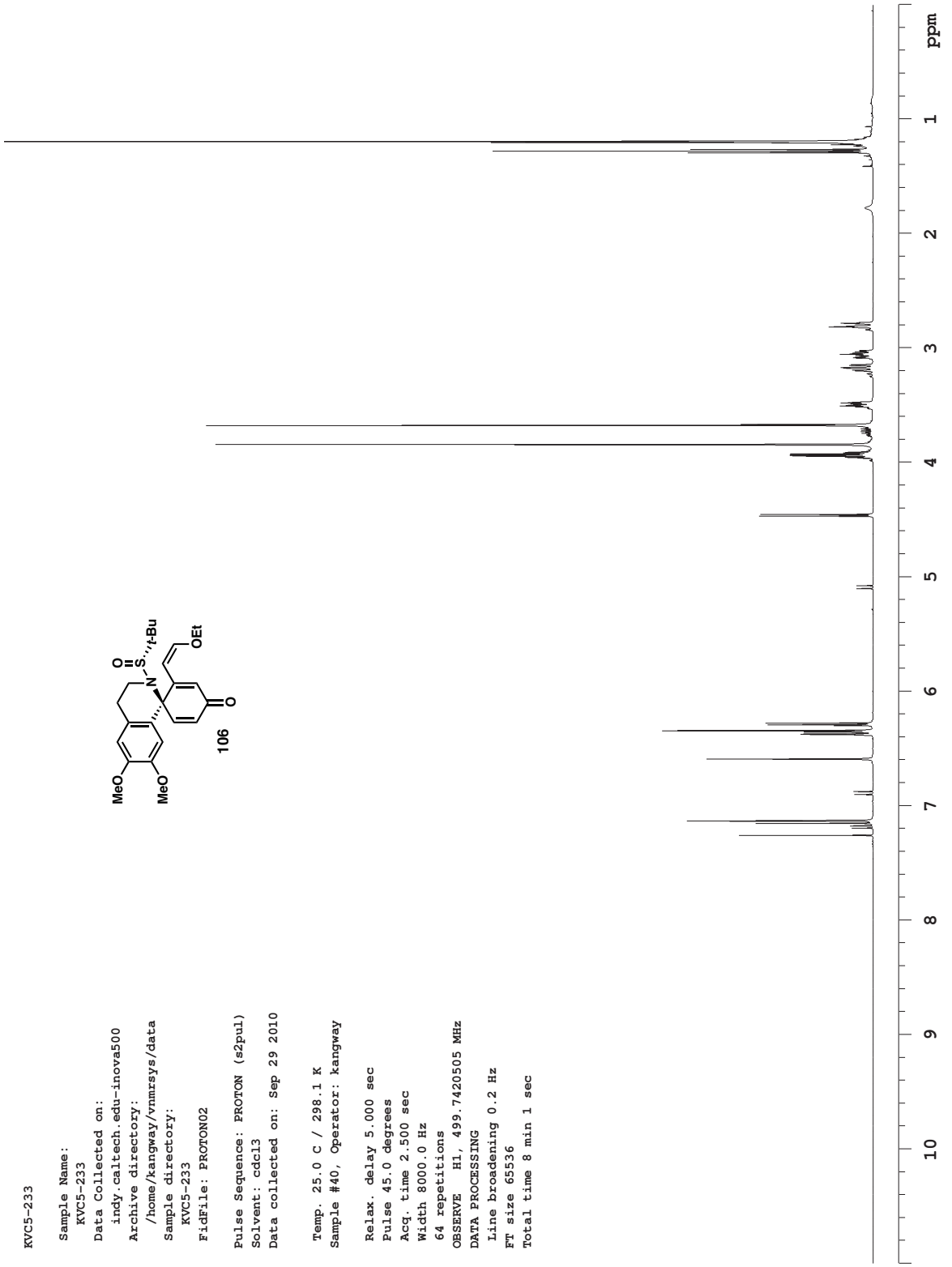
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 21 2010

Temp. 25.0 C / 298.1 K
Sample #34, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6602442 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min



104


KVC5-233
Sample Name:
KVC5-233
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC5-233
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 29 2010
Temp. 25.0 C / 298.1 K
Sample #40, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
64 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 8 min 1 sec
MeO
MeO
O
N
S
t-Bu
OEt
O
106
10
9
8
7
6
5
4
3
2
1
ppm

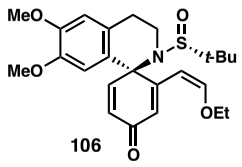
KVC5-233

Sample Name:
KVC5-233
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC5-233
FidFile: CARBON02

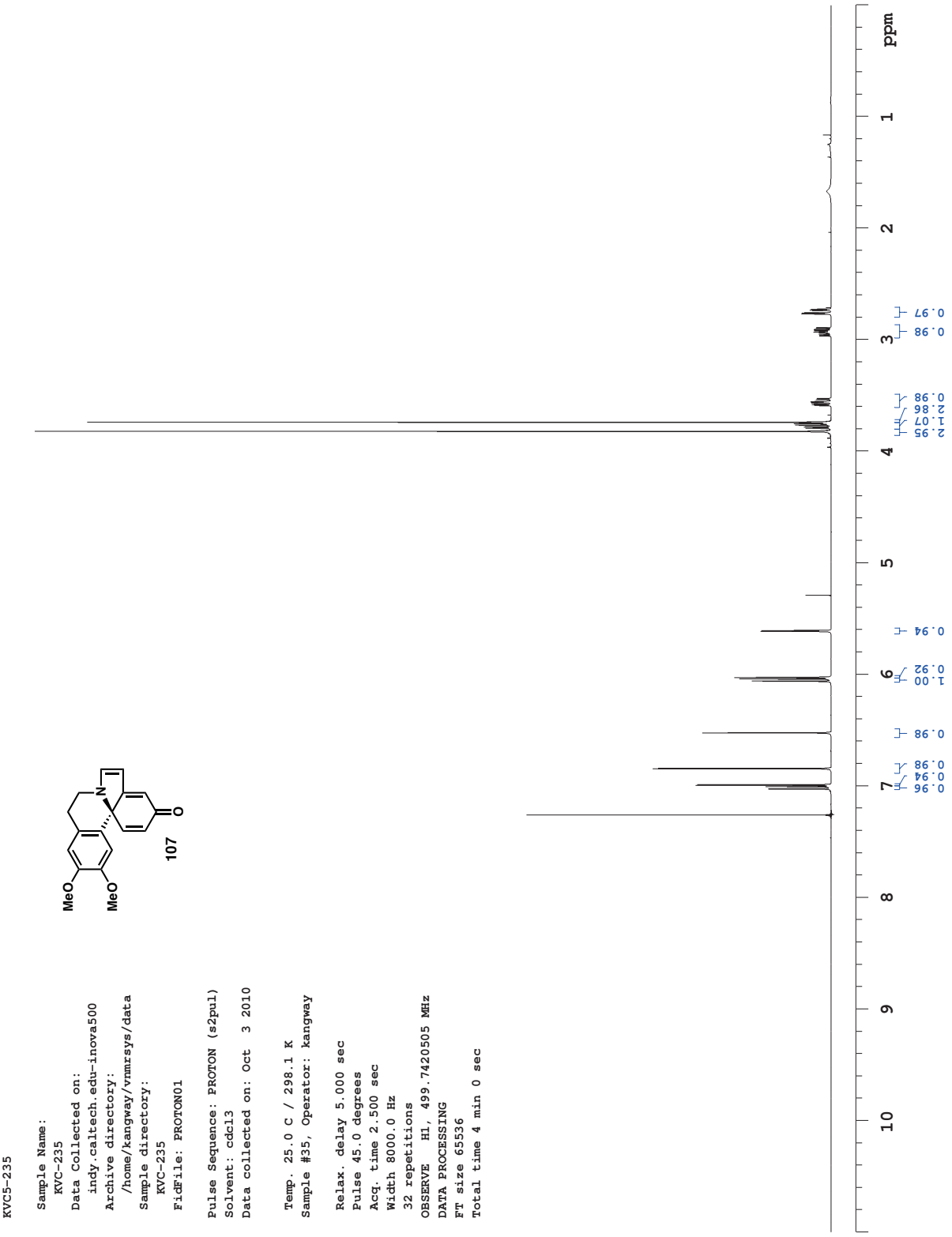
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 29 2010

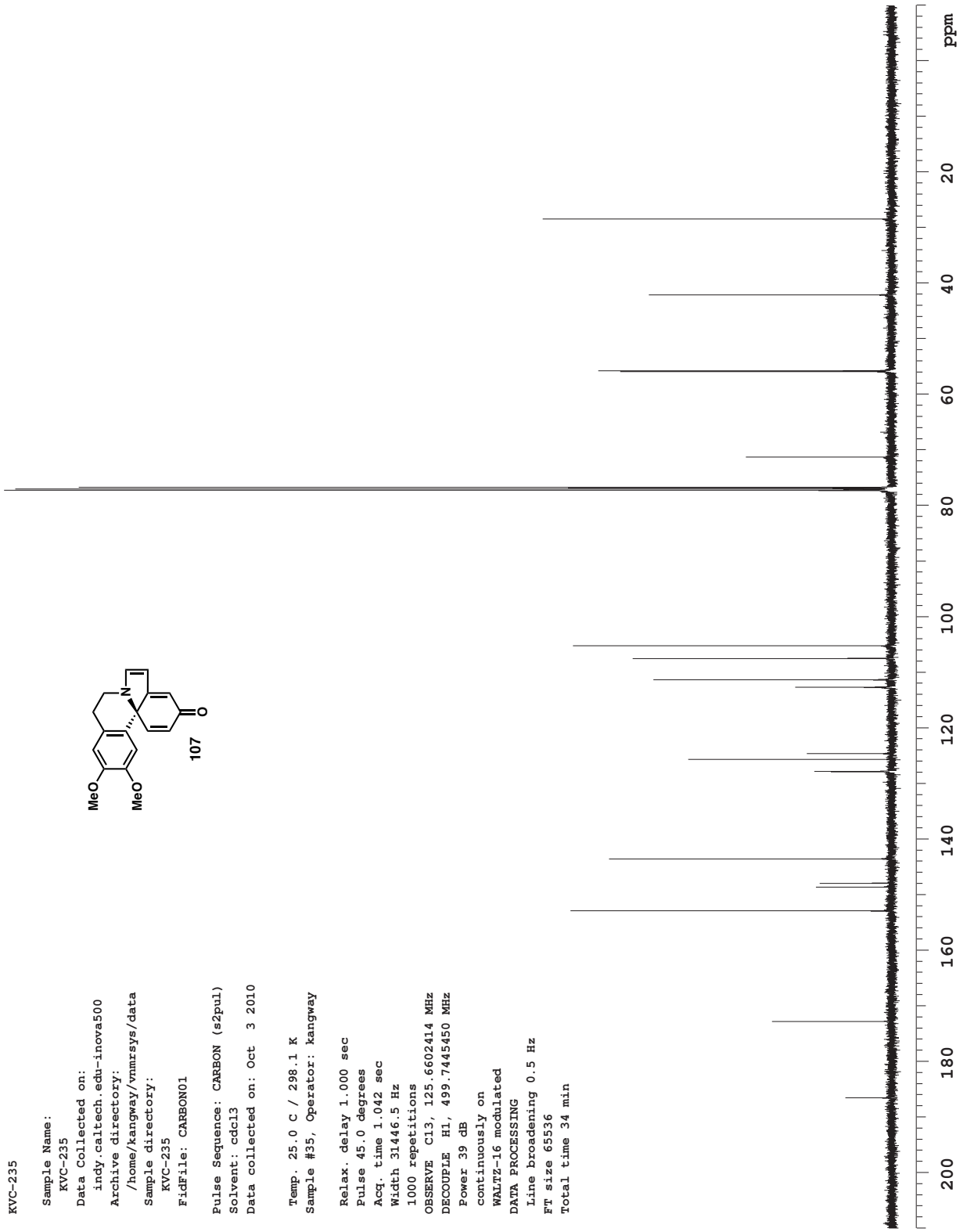
Temp. 25.0 C / 298.1 K
Sample #40, Operator: kangway

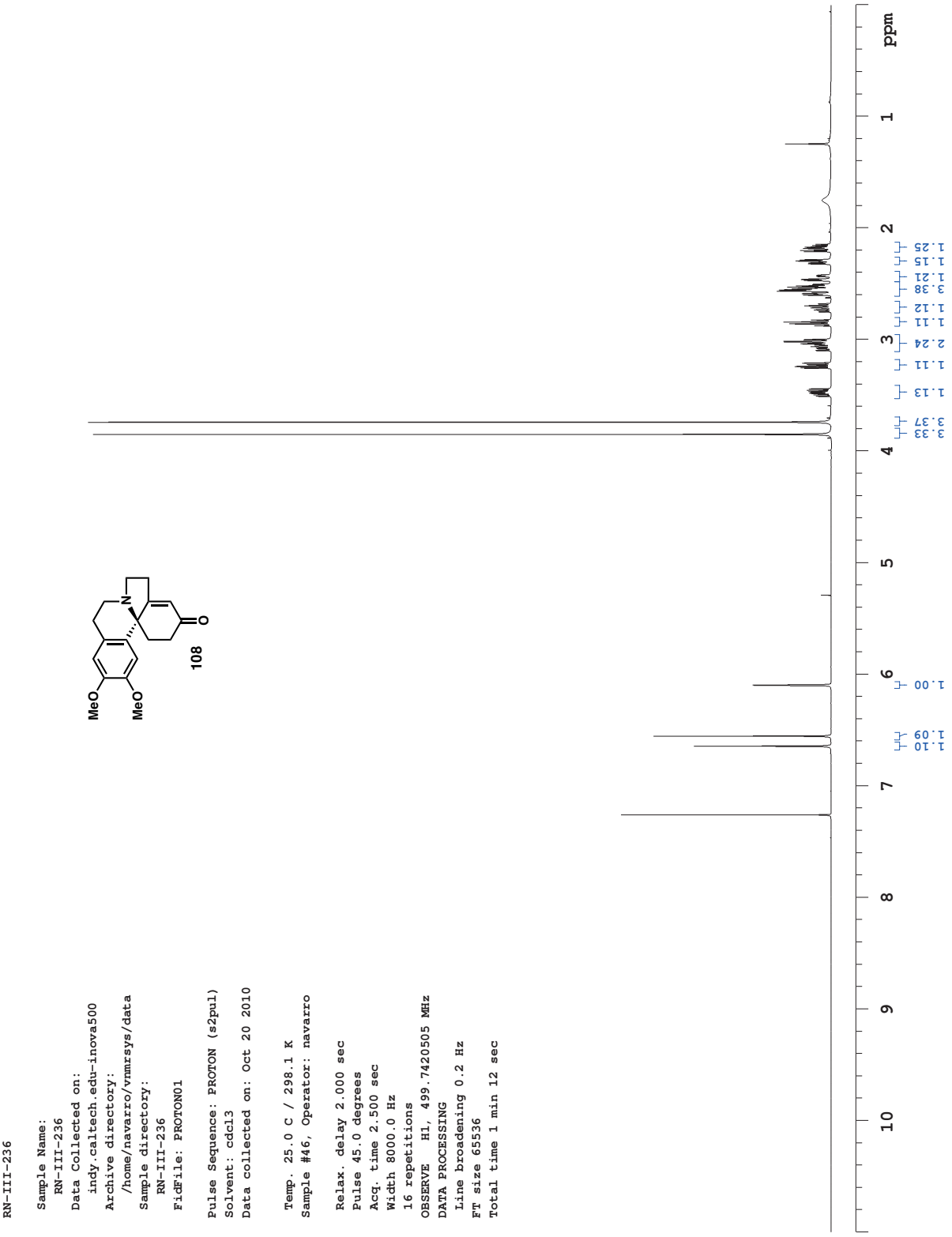
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6602423 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min

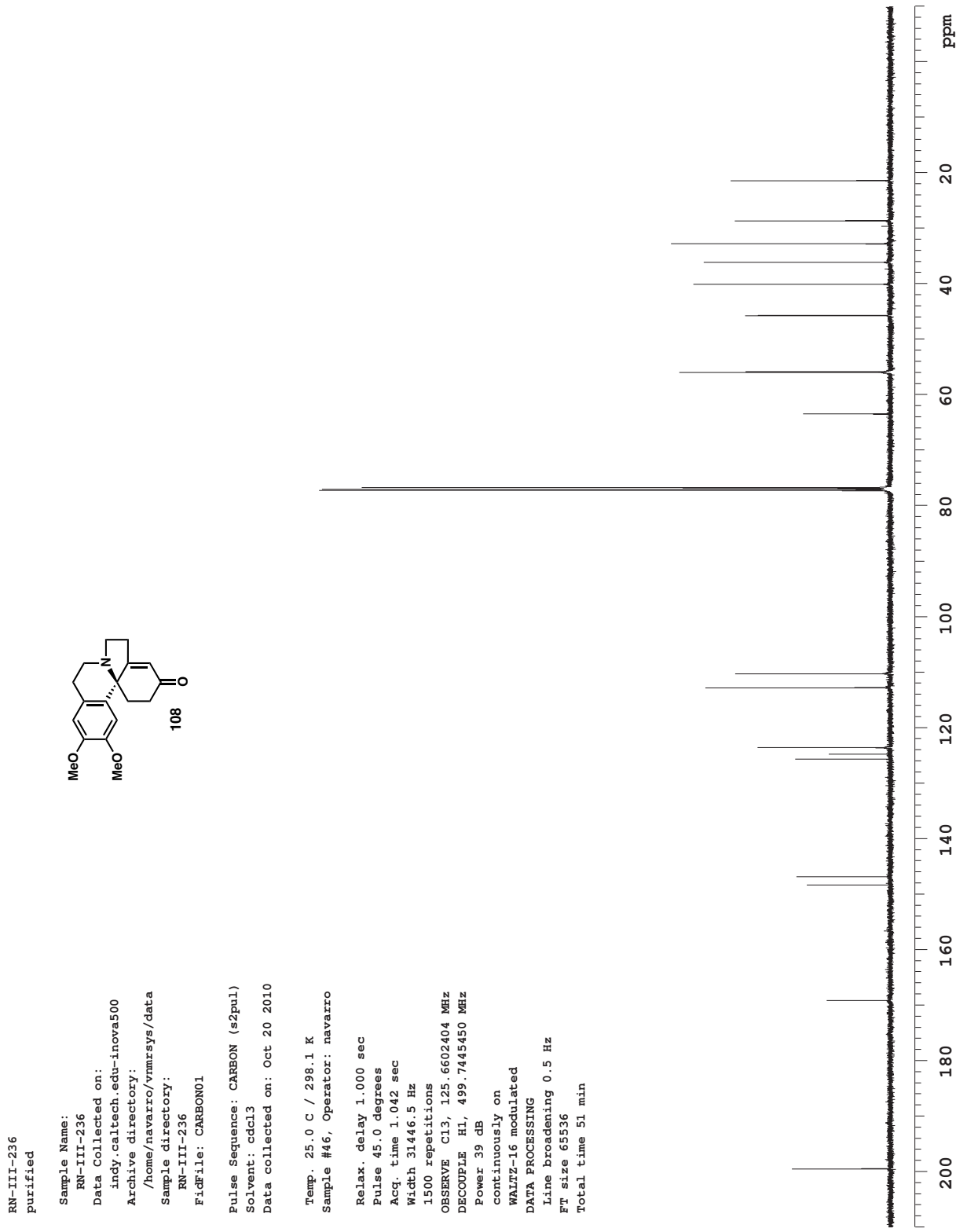


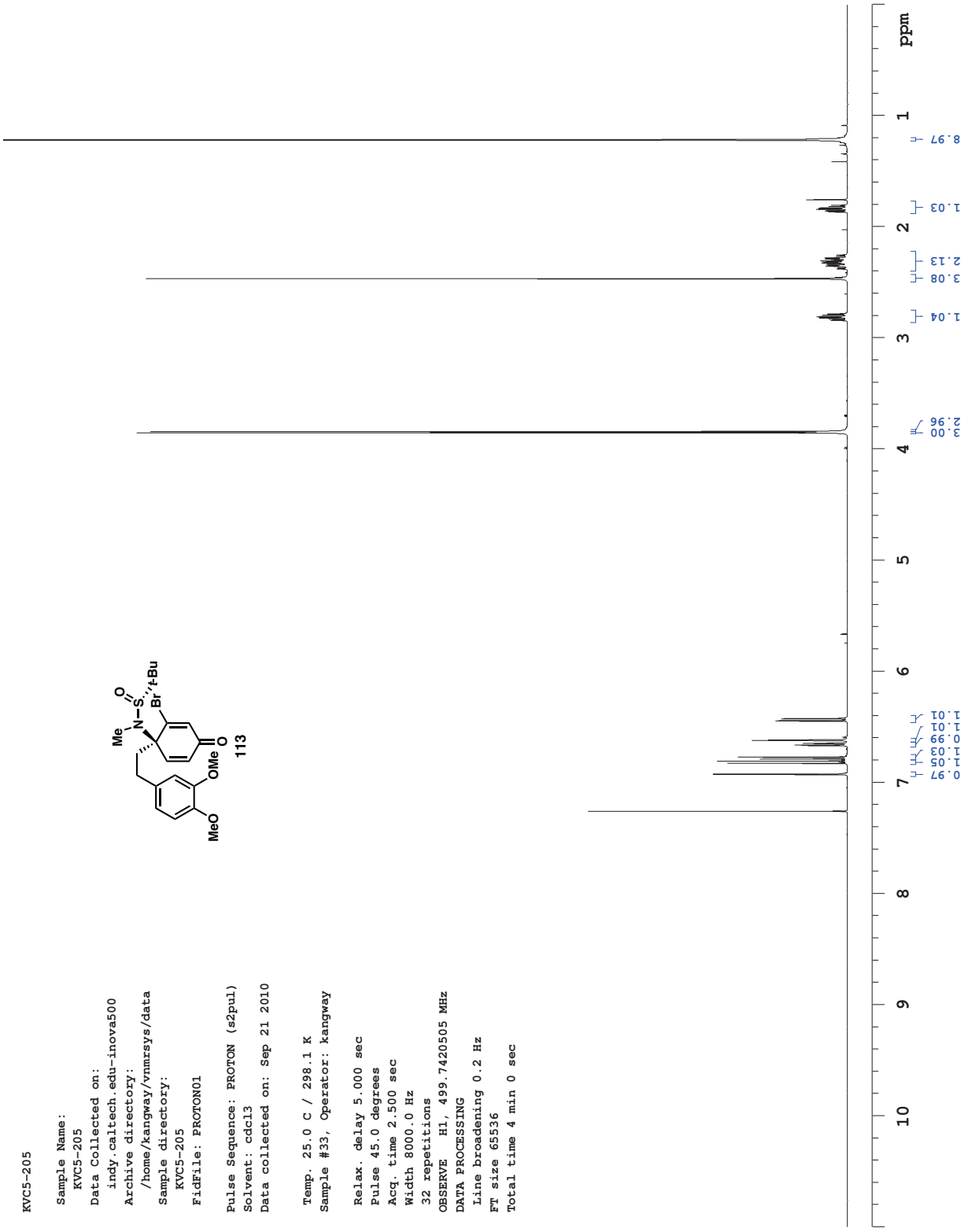
106

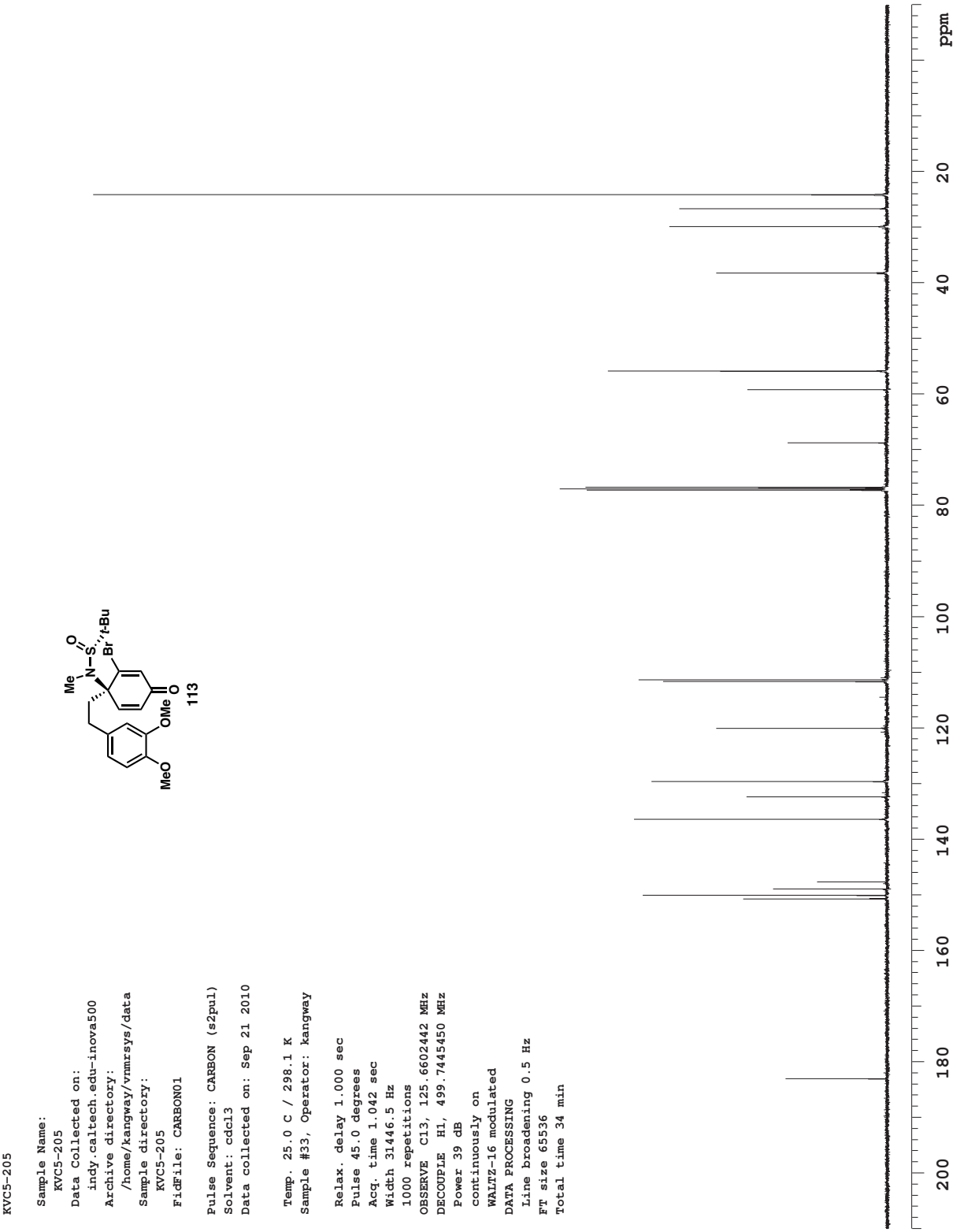

KVC5-235
Sample Name:
KVC-235
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC-235
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 3 2010
Temp. 25.0 C / 298.1 K
Sample #35, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 65536
Total time 4 min 0 sec
MeO
MeO
N
O
107
ppm
0.97
0.98
2.95
1.07
2.86
0.98
0.94
1.00
0.92
0.98
0.96
0.94
0.98

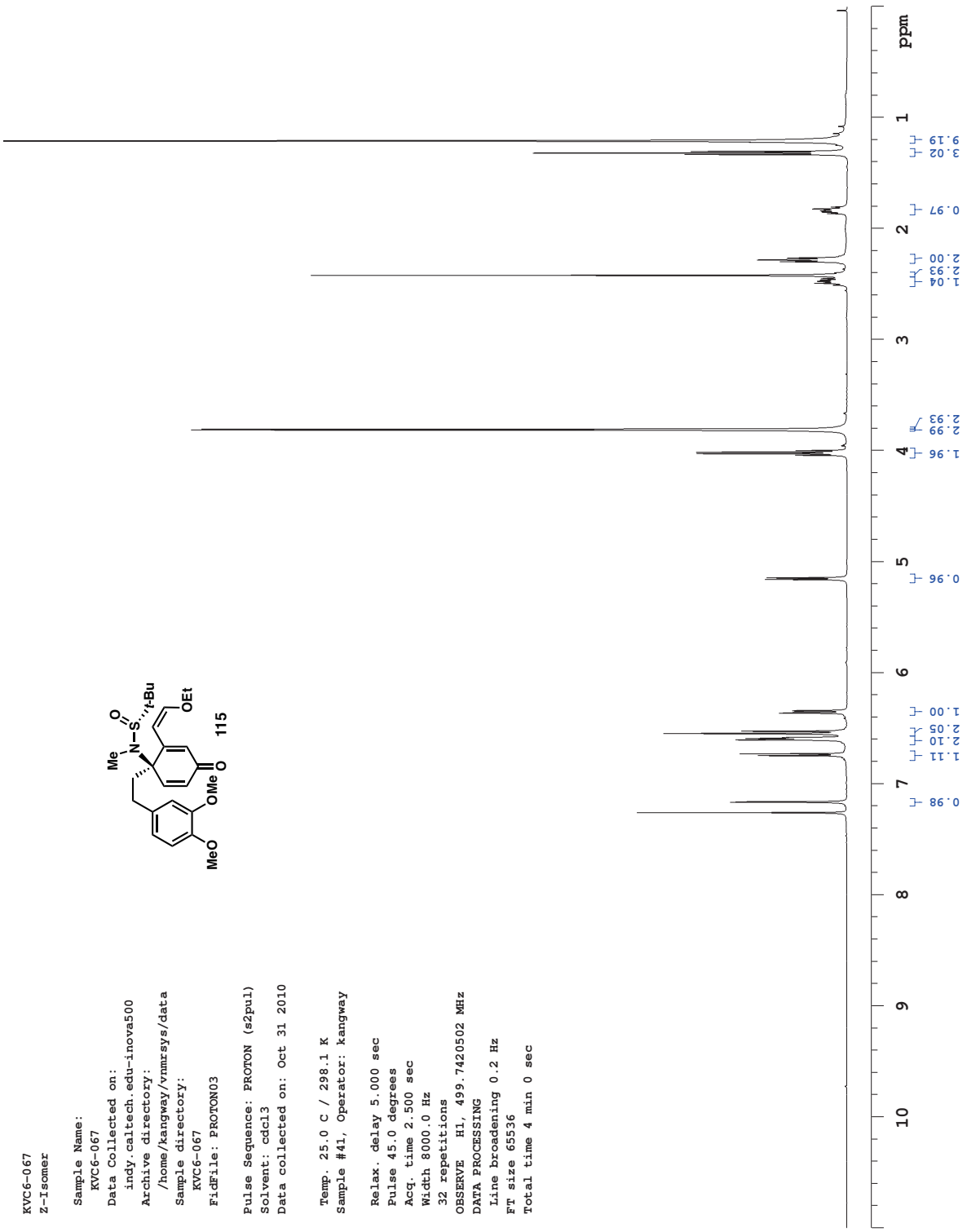

KVC-235
Sample Name:
KVC-235
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC-235
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 3 2010
Temp. 25.0 C / 298.1 K
Sample #35, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6602414 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
MeO
MeO
N
O
107
200
180
160
140
120
100
80
60
40
20
ppm


RN-III-236
Sample Name:
RN-III-236
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-236
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 20 2010
Temp. 25.0 C / 298.1 K
Sample #46, Operator: navarro
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 1 min 12 sec
MeO
MeO
N
O
108
ppm
1
2
3
4
5
6
7
8
9
10
1.25
1.15
3.38
1.21
1.12
1.11
2.24
1.11
1.13
3.37
3.33
1.00
1.10
1.09

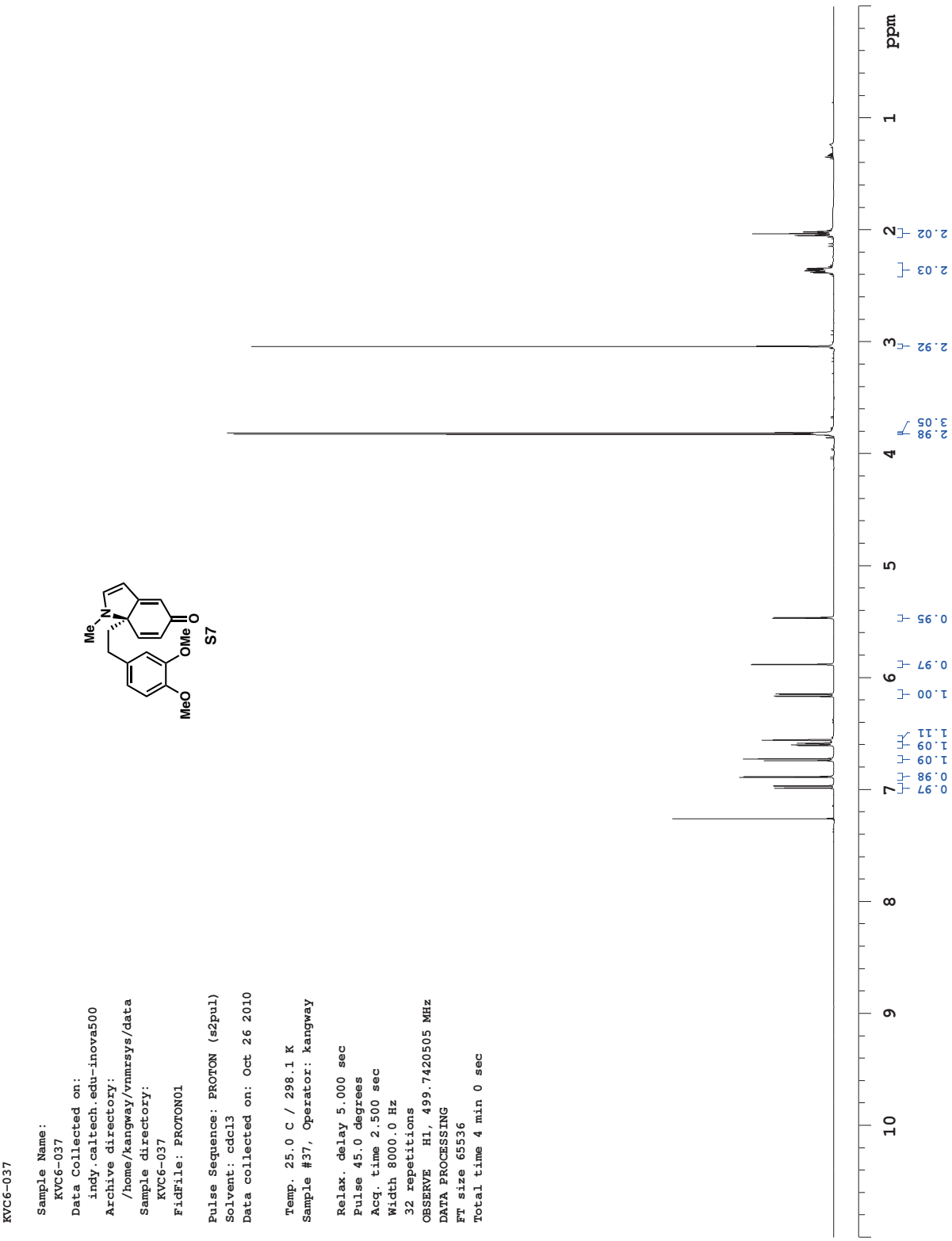

RN-III-236
purified
Sample Name:
RN-III-236
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-III-236
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 20 2010
Temp. 25.0 C / 298.1 K
Sample #46, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6602404 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
MeO
MeO
O
N
108
200
180
160
140
120
100
80
60
40
20
ppm

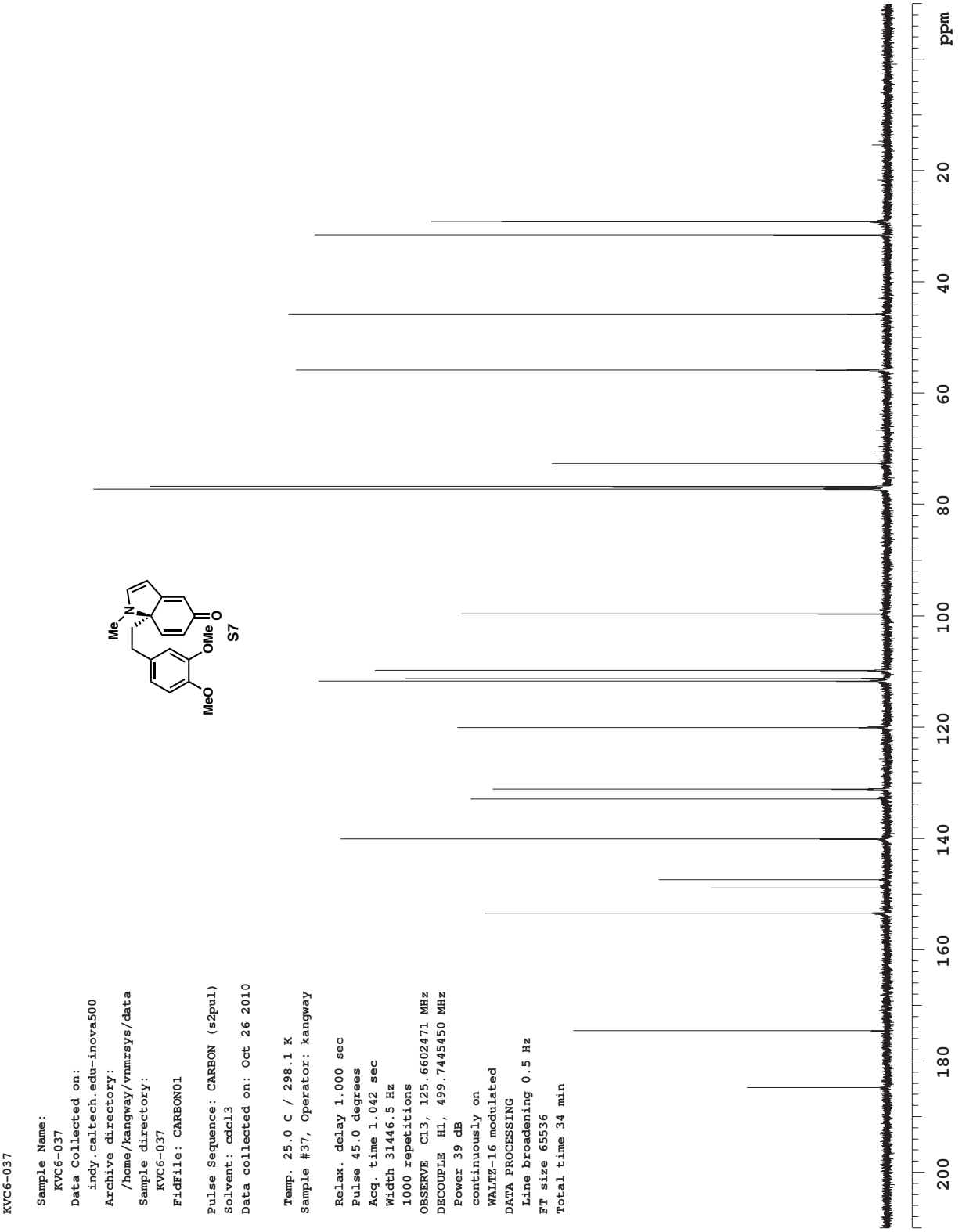

KVC5-205
Sample Name:
KVC5-205
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC5-205
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 21 2010
Temp. 25.0 C / 298.1 K
Sample #33, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Me
N
S
O
t-Bu
Br
OMe
O
MeO
113
ppm
10
9
8
7
6
5
4
3
2
1
0.97
1.05
1.03
0.99
1.01
1.01
3.00
2.96
1.04
3.08
2.13
1.03
8.97

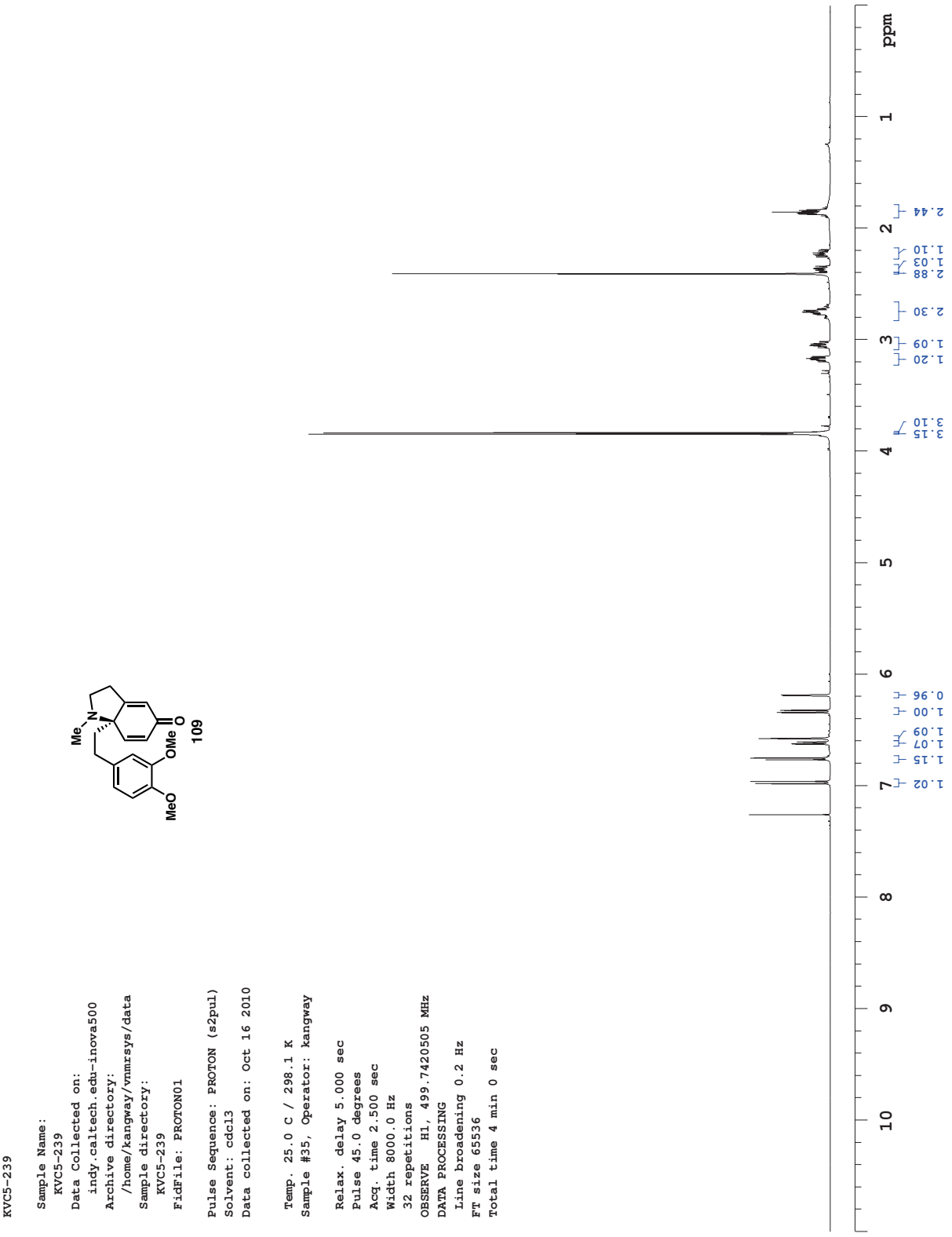

KVC5-205
Sample Name:
KVC5-205
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC5-205
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 21 2010
Temp. 25.0 C / 298.1 K
Sample #33, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6602442 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
Me
O
N
S
Br
t-Bu
OMe
O
MeO
113
200
180
160
140
120
100
80
60
40
20
ppm

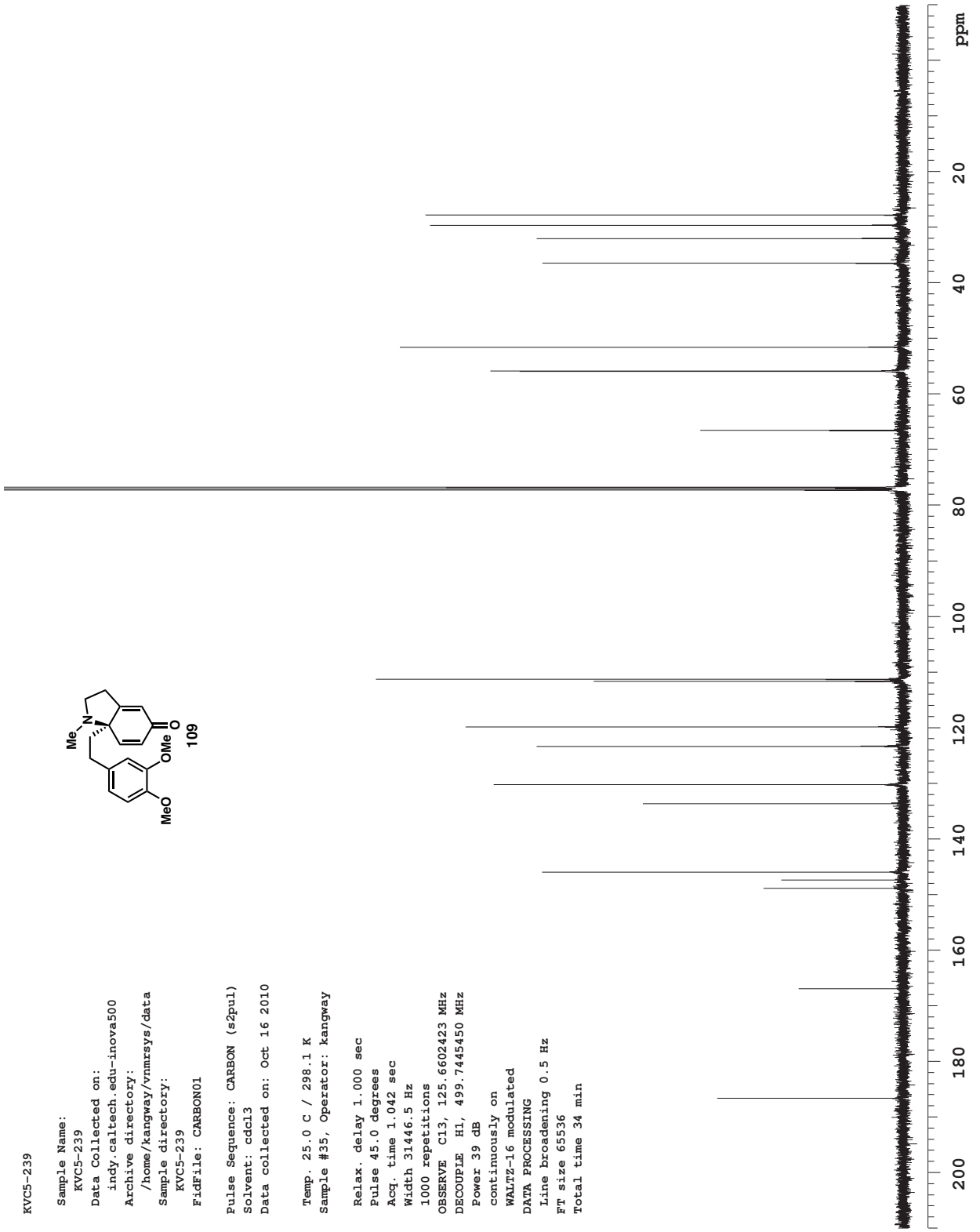

KVC6-067
Z-Isomer
Sample Name:
KVC6-067
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC6-067
FidFile: PROTON03
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 31 2010
Temp. 25.0 C / 298.1 K
Sample #41, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7420502 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Me
O
N
S
t-Bu
OEt
MeO
OMe
O
115
ppm
1
2
3
4
5
6
7
8
9
10
9.19
3.02
0.97
2.00
2.93
1.04
2.99
2.93
1.96
0.96
1.00
2.05
2.10
1.11
0.98

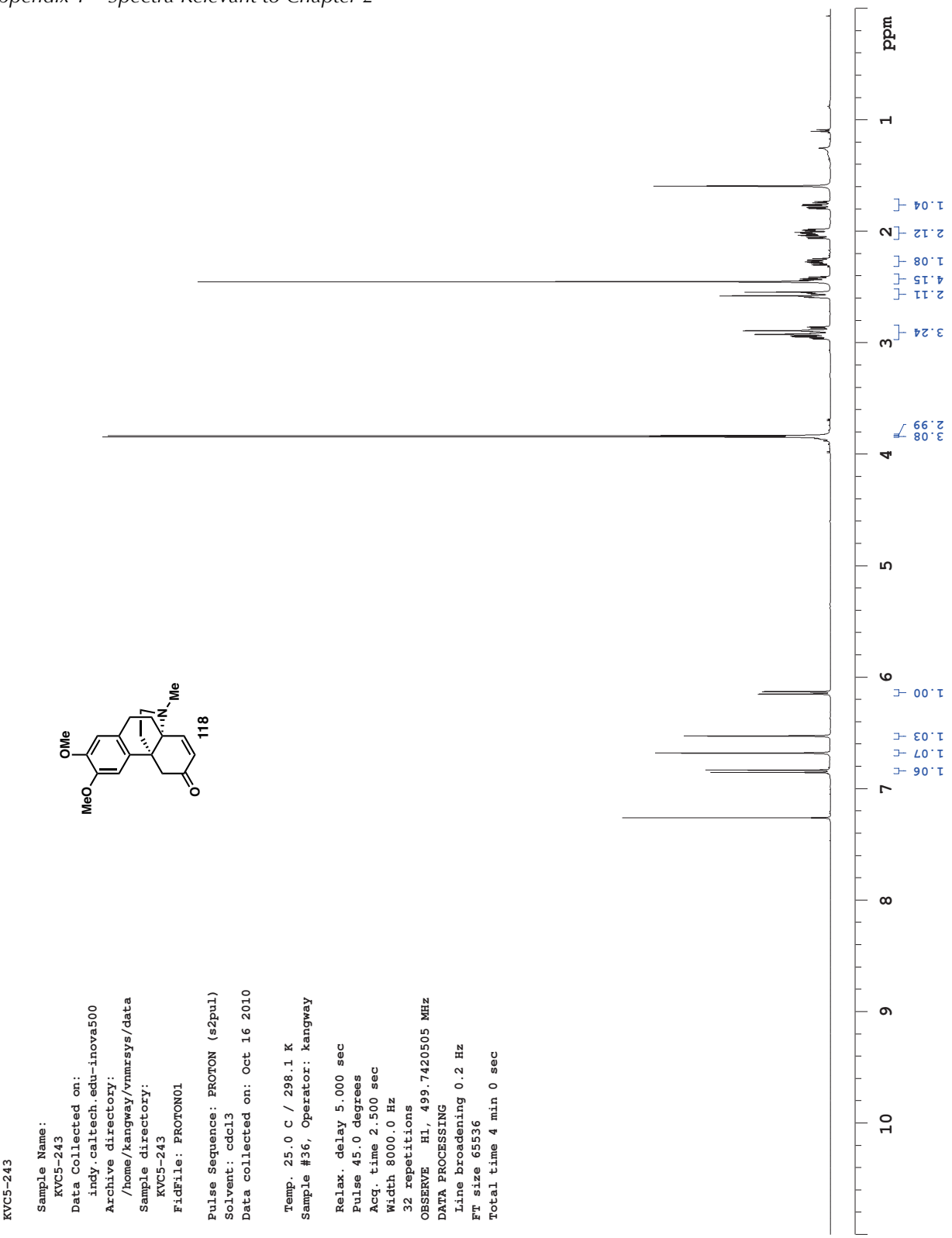
KVC6-067
Z-Isomer
Sample Name:
KVC6-067
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC6-067
FidFile: CARBON02
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 31 2010
Temp. 25.0 C / 298.1 K
Sample #41, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6602500 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
Me
O
N
S
t-Bu
OEt
OMe
O
MeO
115
200
180
160
140
120
100
80
60
40
20
ppm

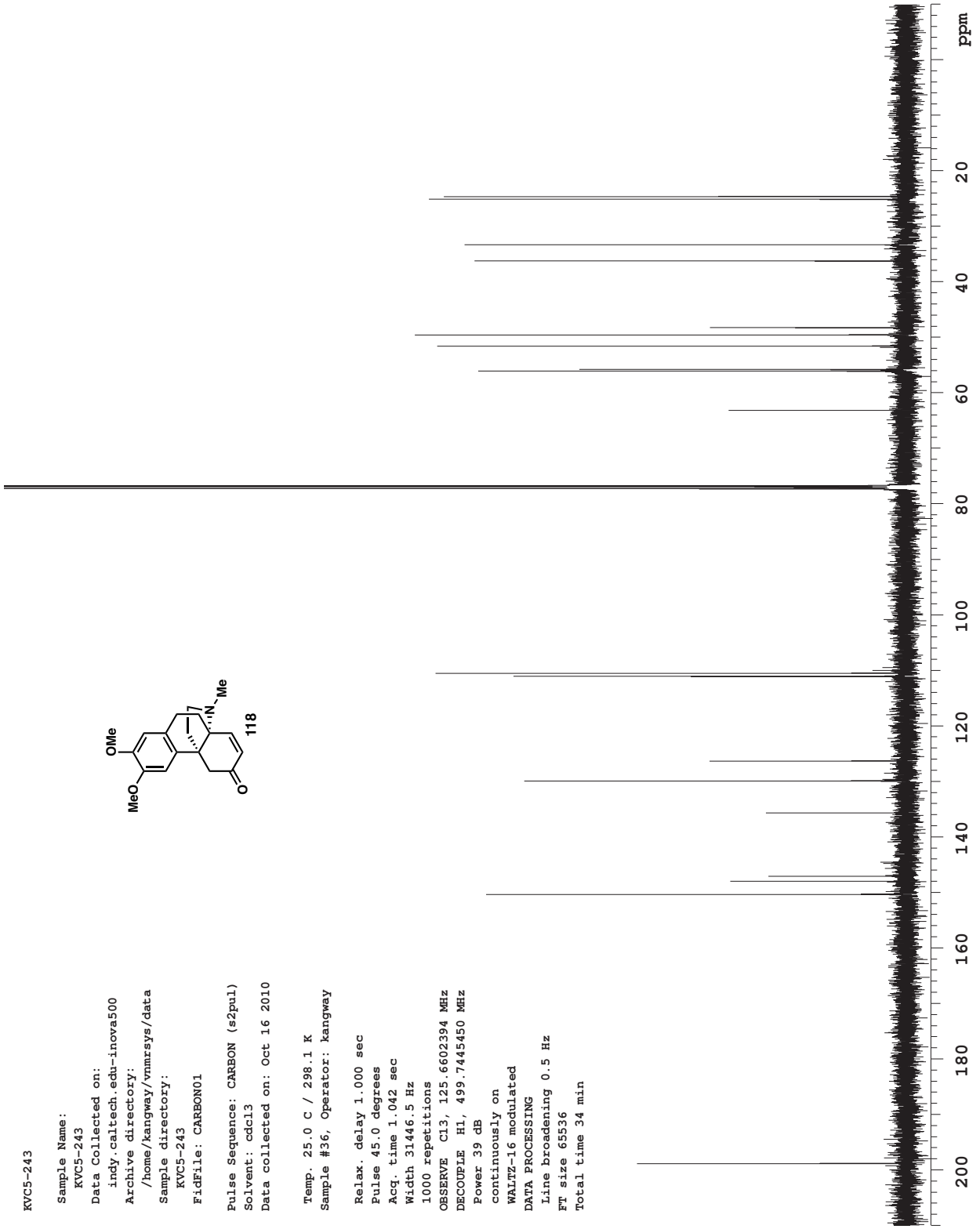

KVC6-037
Sample Name:
KVC6-037
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC6-037
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 26 2010
Temp. 25.0 C / 298.1 K
Sample #37, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 65536
Total time 4 min 0 sec
Me
N
OMe
O
MeO
S7
ppm
10
9
8
7
6
5
4
3
2
1
0.97
0.98
1.09
1.09
1.11
1.00
0.97
0.95
2.98
3.05
2.92
2.03
2.02

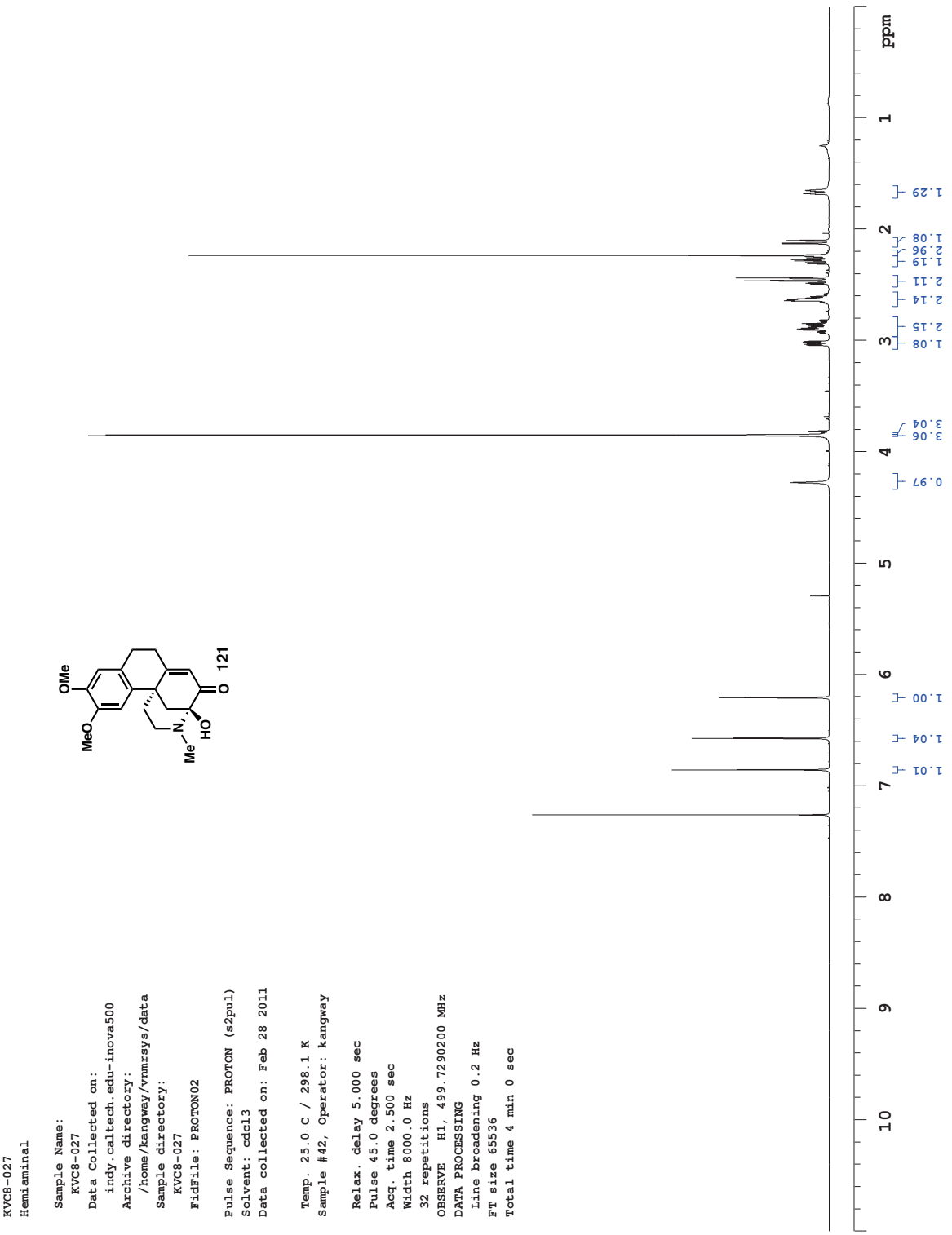

KVC6-037
Sample Name:
KVC6-037
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC6-037
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 26 2010
Temp. 25.0 C / 298.1 K
Sample #37, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6602471 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
Me
N
OMe
O
MeO
S7
200
180
160
140
120
100
80
60
40
20
ppm

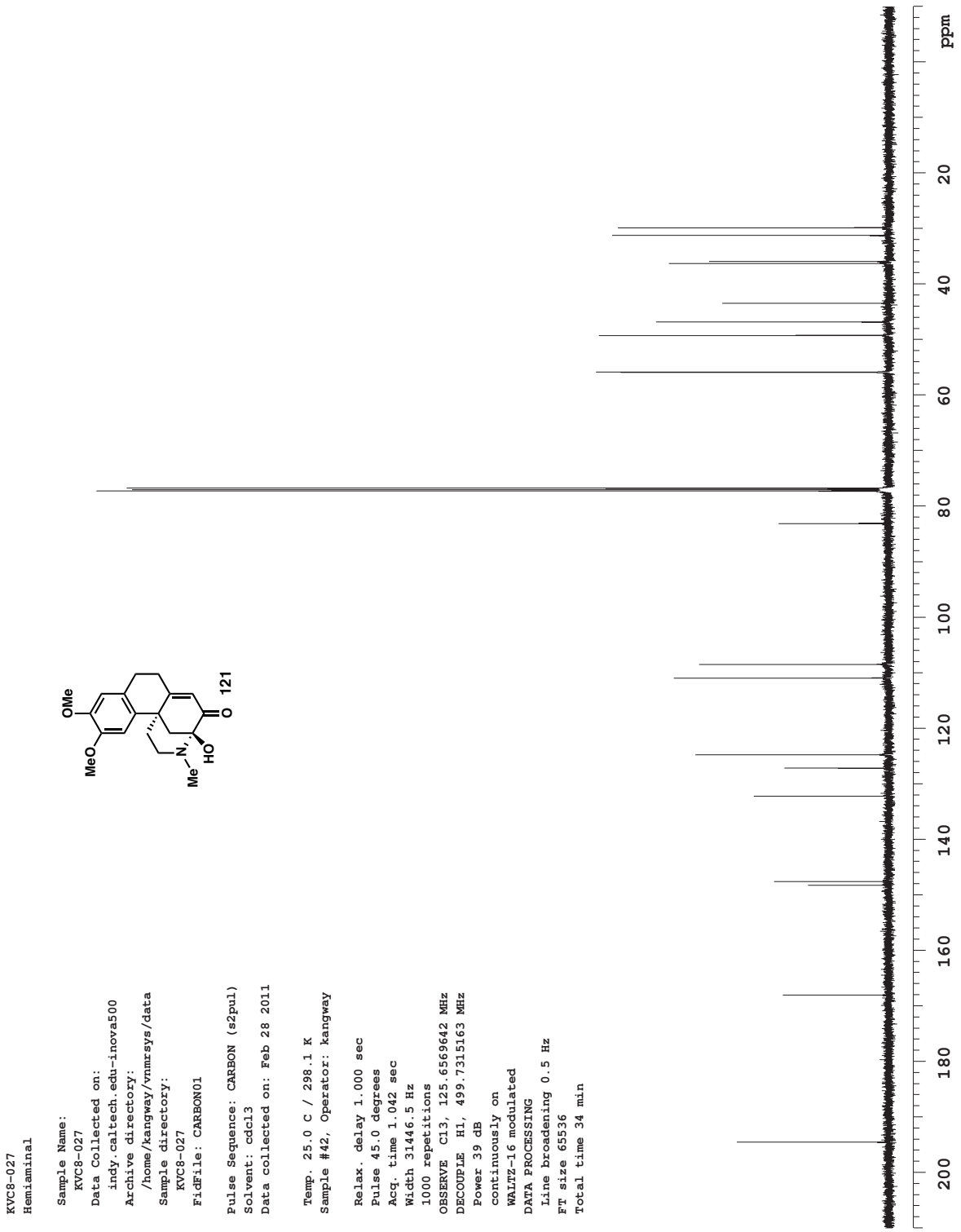

KVC5-239
Sample Name:
KVC5-239
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC5-239
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 16 2010
Temp. 25.0 C / 298.1 K
Sample #35, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Me
N
OMe
O
MeO
109
ppm
1.02
1.15
1.07
1.09
1.00
0.96
3.10
3.15
1.20
1.09
2.30
2.88
1.03
1.10
2.44

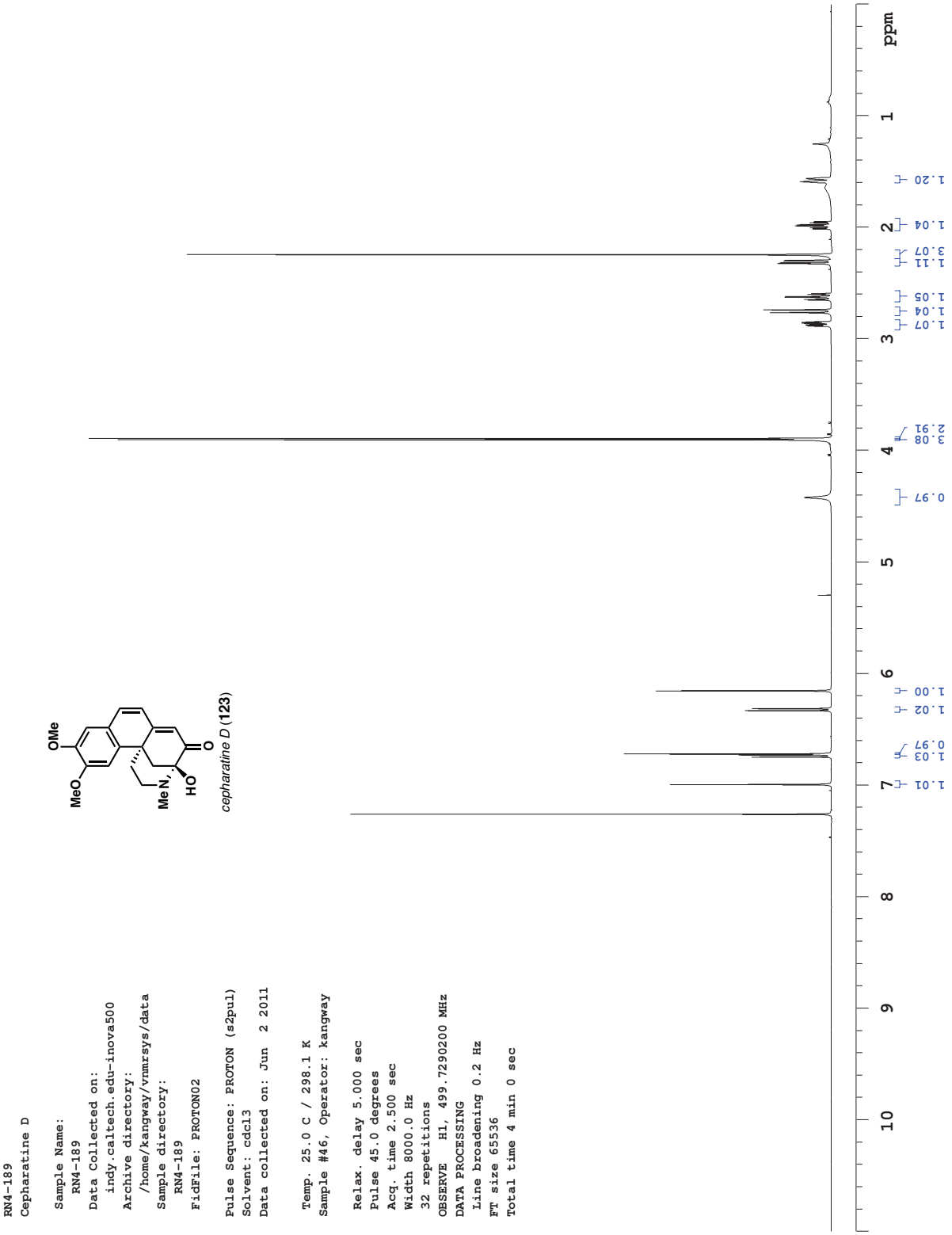

KVC5-239
Sample Name:
KVC5-239
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC5-239
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 16 2010
Temp. 25.0 C / 298.1 K
Sample #35, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6602423 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
Me
N
OMe
O
MeO
109
200
180
160
140
120
100
80
60
40
20
ppm

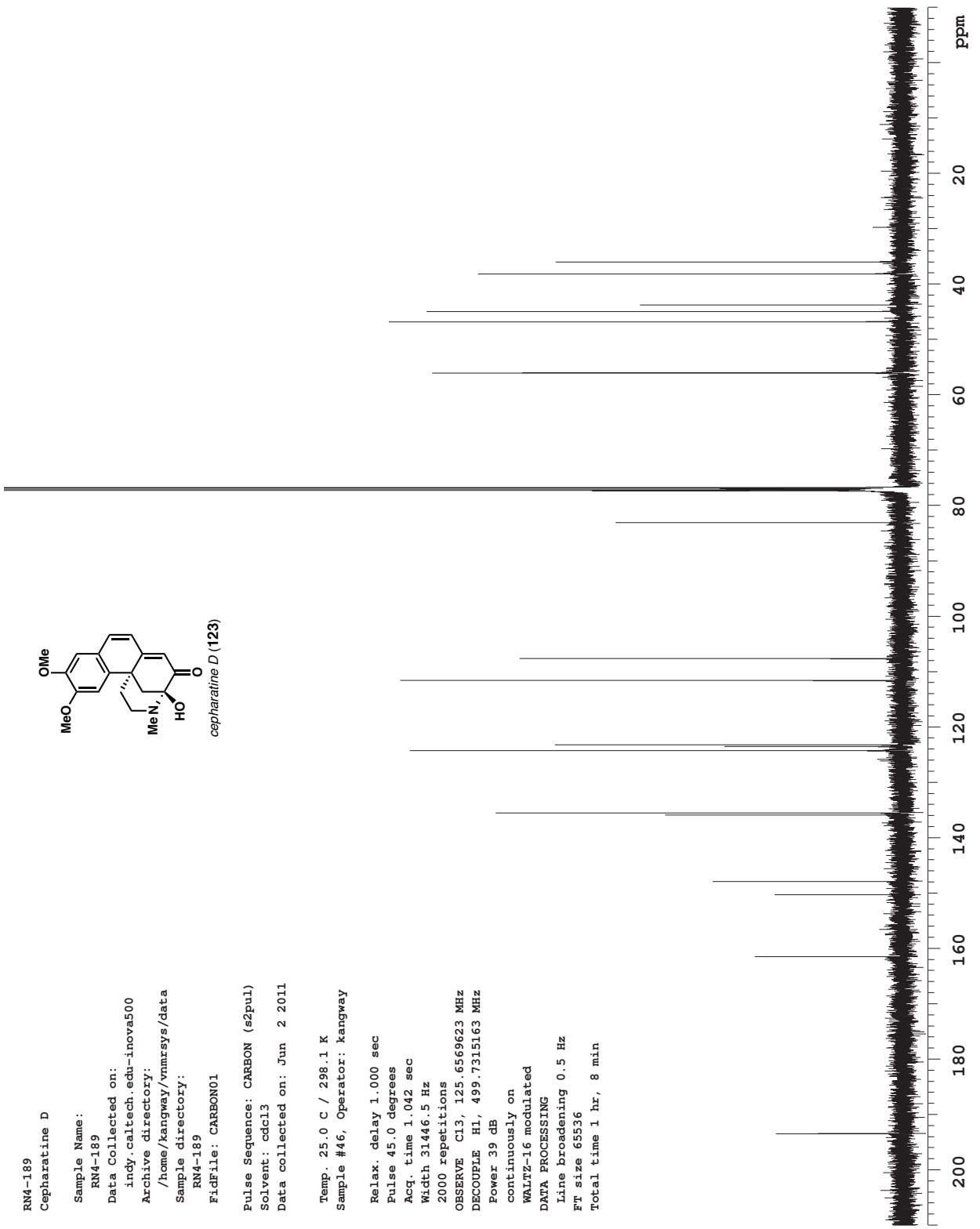

KVC5-243
Sample Name:
KVC5-243
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC5-243
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 16 2010
Temp. 25.0 C / 298.1 K
Sample #36, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
OMe
MeO
N
Me
O
118
ppm
1.00
1.03
1.07
1.06
3.08
2.99
3.24
2.11
4.15
1.08
2.12
1.04

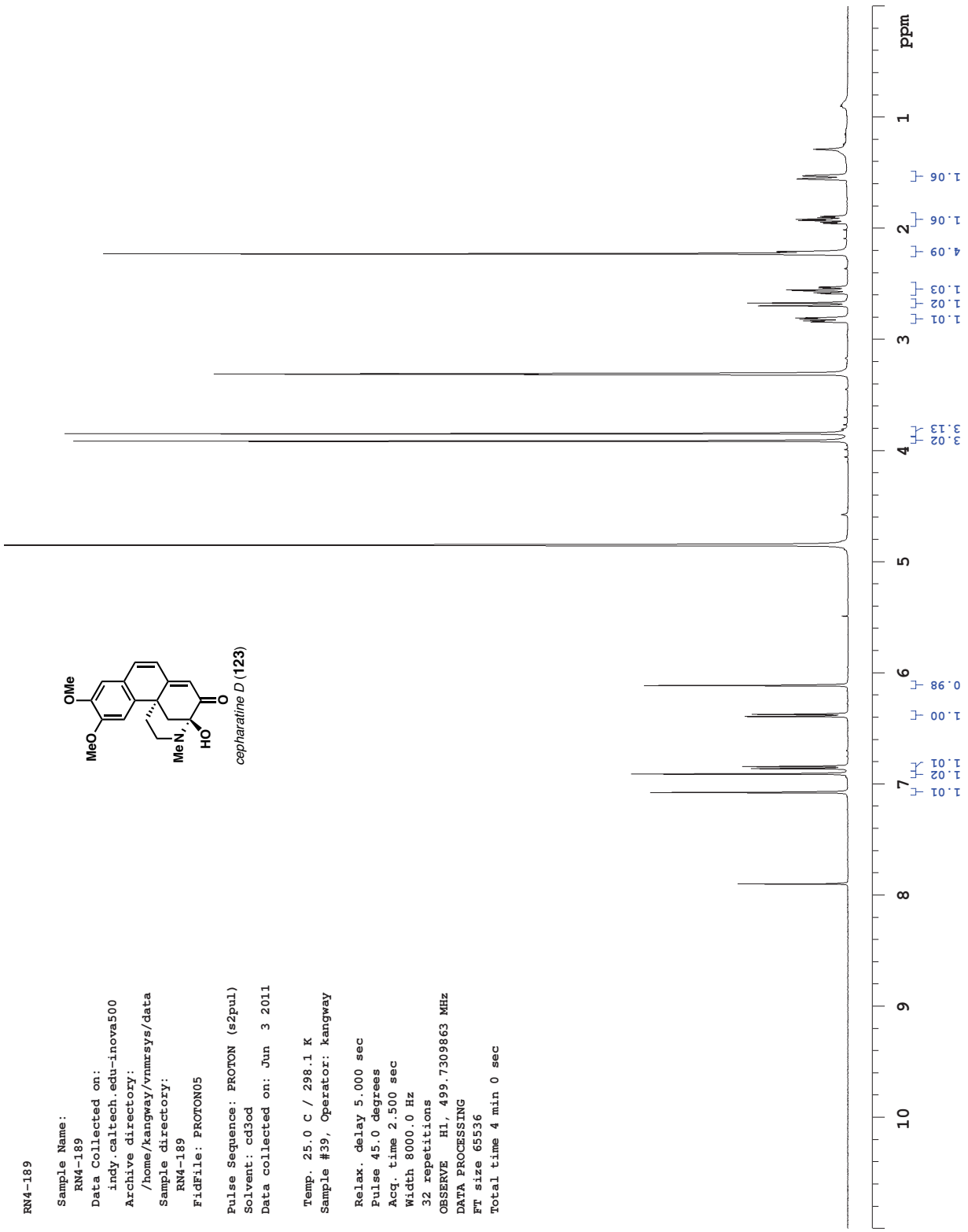

KVC5-243
Sample Name:
KVC5-243
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC5-243
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 16 2010
Temp. 25.0 C / 298.1 K
Sample #36, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6602394 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
OMe
MeO
N
Me
O
118
200
180
160
140
120
100
80
60
40
20
ppm

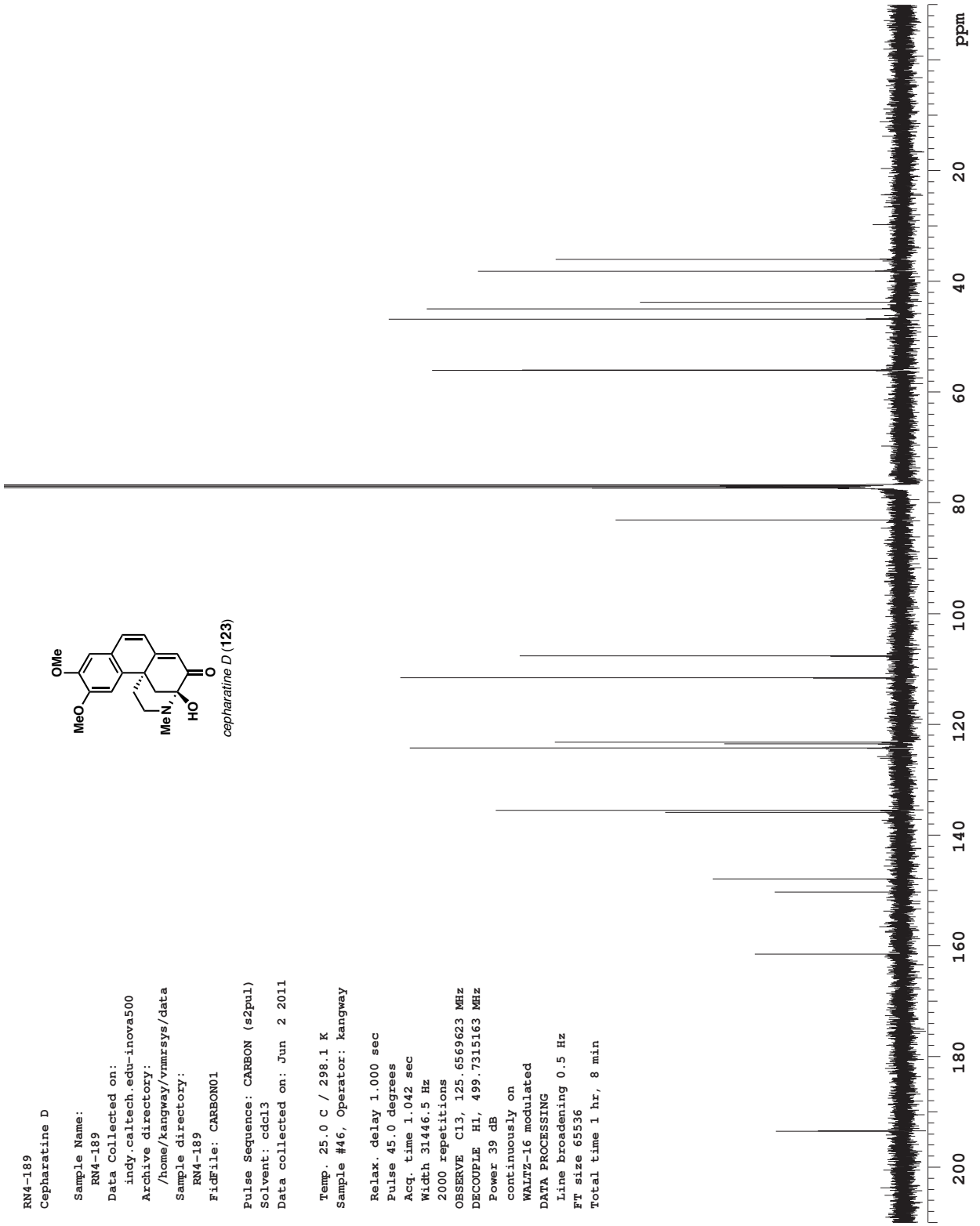

KVC8-027
Hemiaminal
Sample Name:
KVC8-027
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC8-027
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Feb 28 2011
Temp. 25.0 C / 298.1 K
Sample #42, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290200 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
OMe
MeO
N
Me
HO
O
121
ppm
1.29
1.08
2.96
1.19
2.11
2.14
2.15
1.08
3.06
3.04
0.97
1.00
1.04
1.01

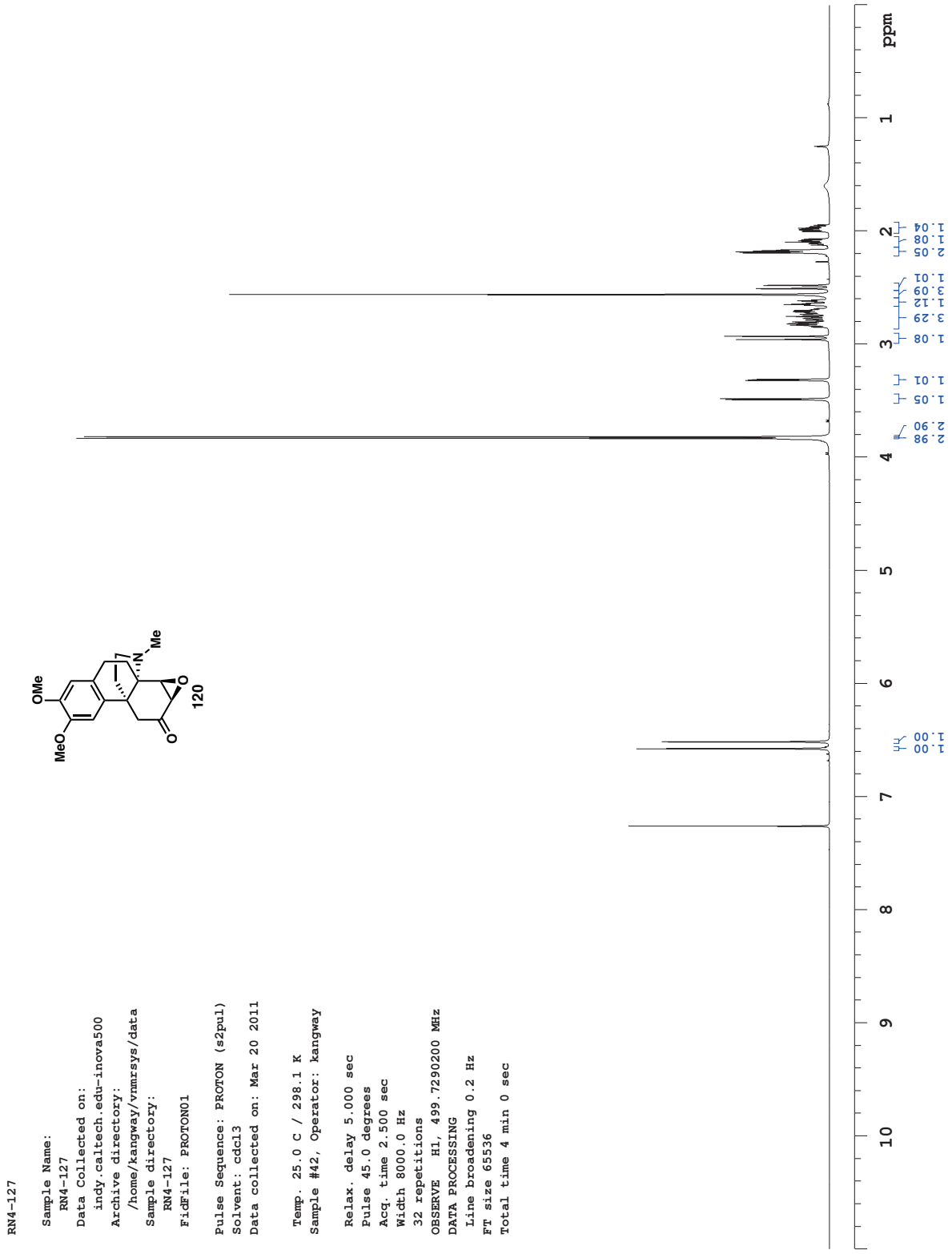

KVC8-027
Hemiaminal
Sample Name:
KVC8-027
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC8-027
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Feb 28 2011
Temp. 25.0 C / 298.1 K
Sample #42, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6569642 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
OMe
MeO
Me
HO
O
121
200
180
160
140
120
100
80
60
40
20
ppm

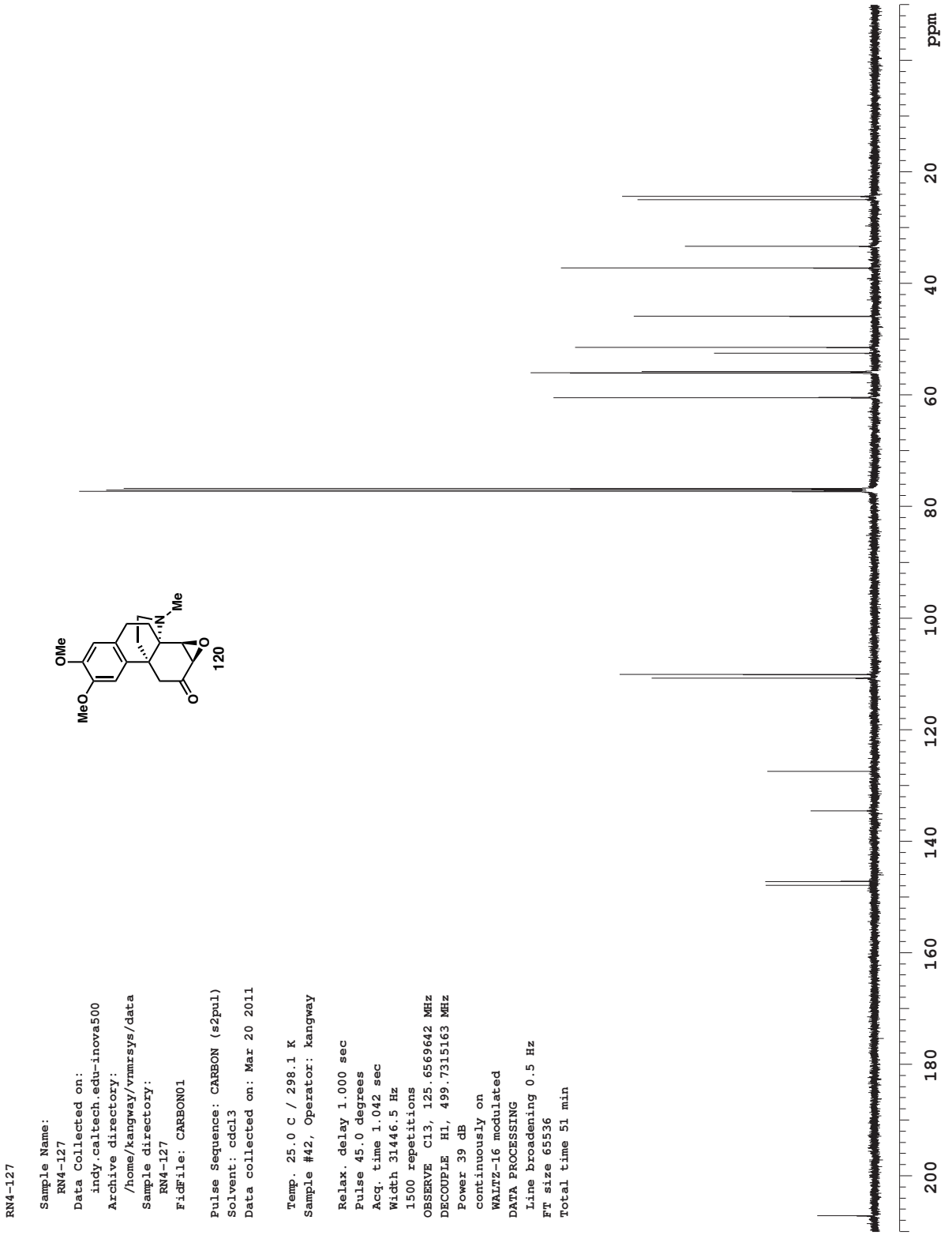

RN4-189
Cepharatine D
Sample Name:
RN4-189
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
RN4-189
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 2 2011
Temp. 25.0 C / 298.1 K
Sample #46, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290200 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
OMe
MeO
MeN
HO
O
cepharatine D (123)
ppm
10
9
8
7
6
5
4
3
2
1
1.01
0.97
1.03
1.02
1.00
0.97
3.08
2.91
1.07
1.04
1.05
1.11
3.07
1.04
1.20

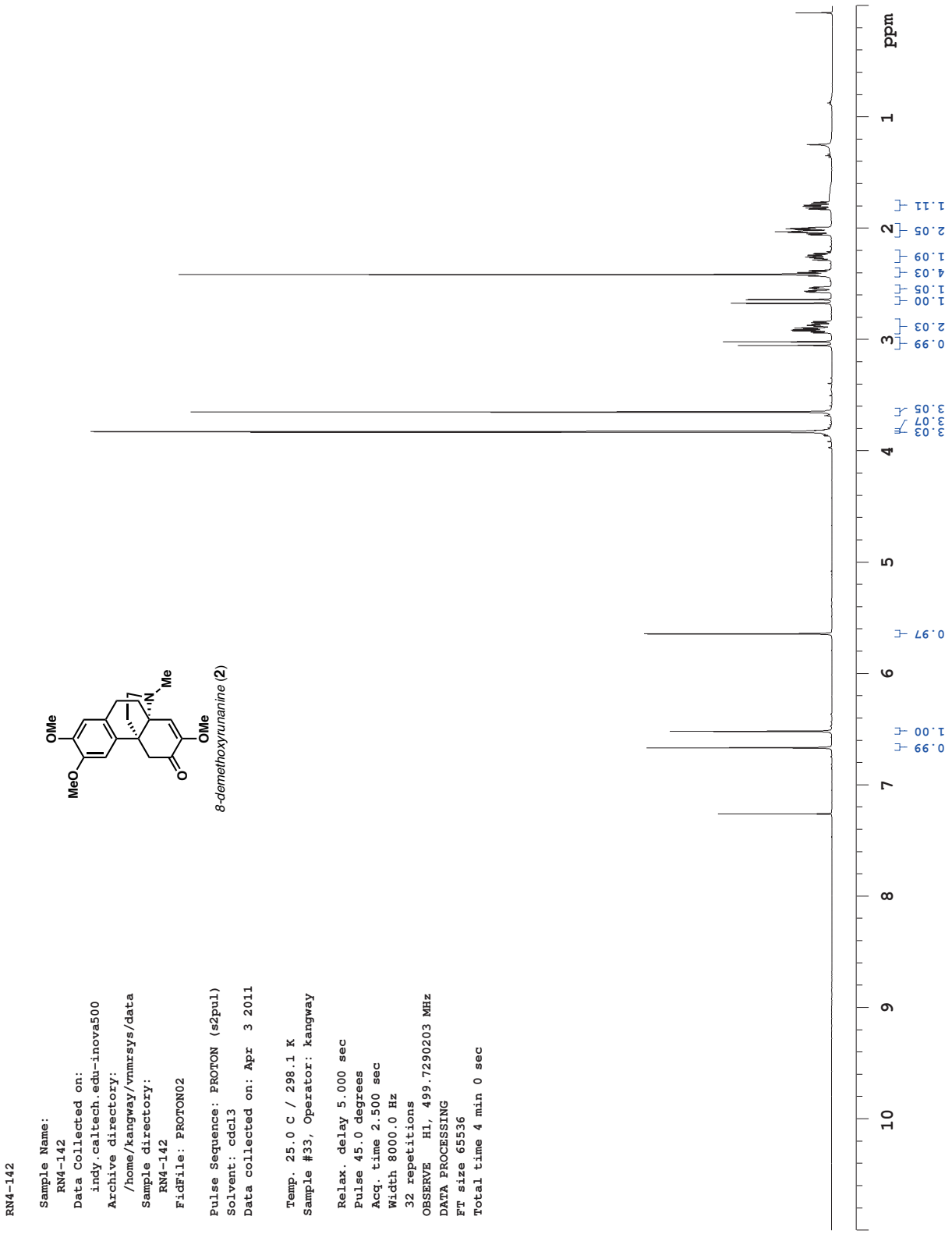

RN4-189
Cepharatine D
Sample Name:
RN4-189
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
RN4-189
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 2 2011
Temp. 25.0 C / 298.1 K
Sample #46, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2000 repetitions
OBSERVE C13, 125.6569623 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 8 min
OMe
MeO
Me N
HO
O
cepharatine D (123)
200
180
160
140
120
100
80
60
40
20
ppm

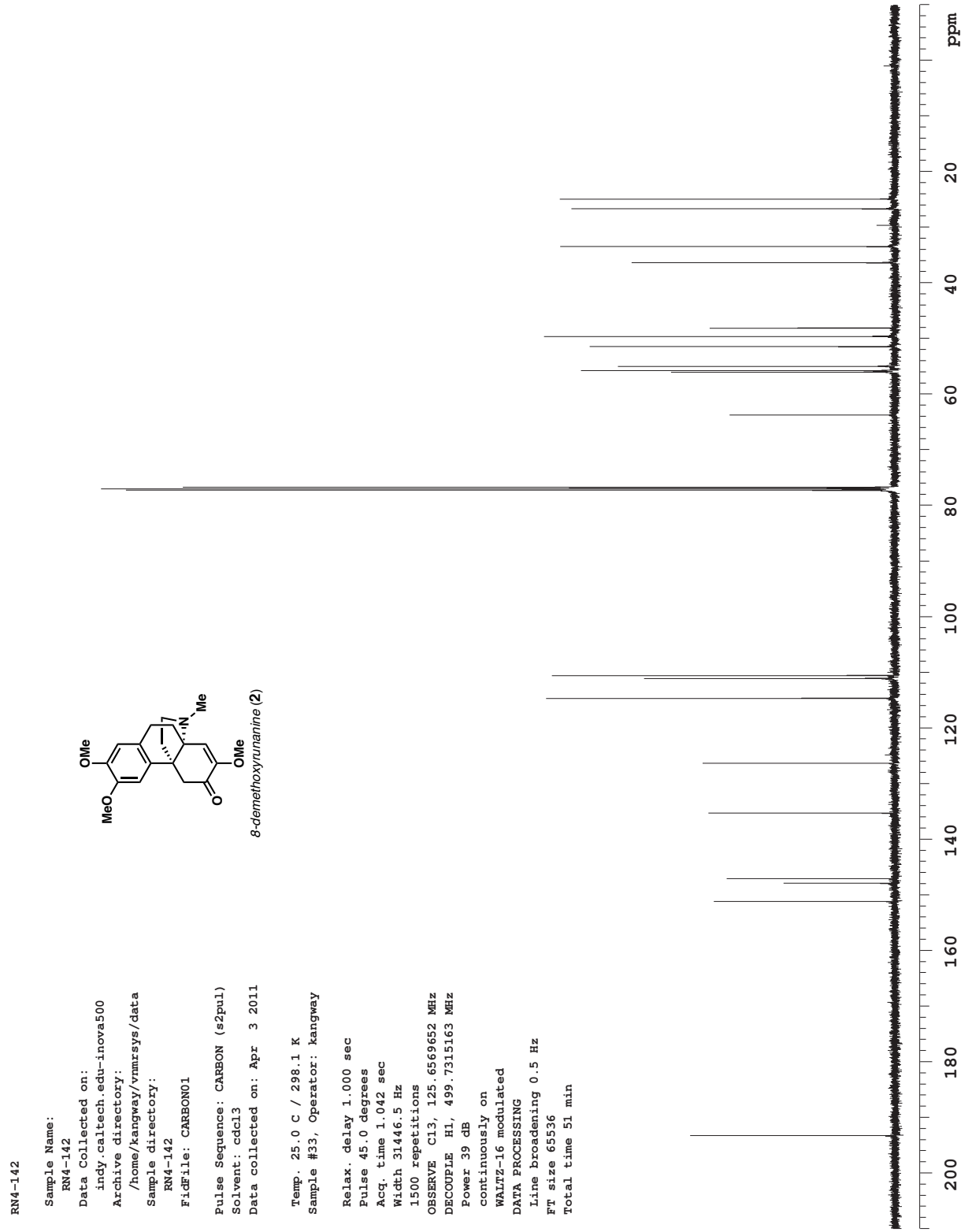

RN4-189
Sample Name:
RN4-189
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
RN4-189
FidFile: PROTON05
Pulse Sequence: PROTON (s2pul)
Solvent: cd3od
Data collected on: Jun 3 2011
Temp. 25.0 C / 298.1 K
Sample #39, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7309863 MHz
DATA PROCESSING
FT size 65536
Total time 4 min 0 sec
OMe
MeO
Me N
HO
O
cepharatine D (123)
ppm
1.06
1.06
4.09
1.03
1.02
1.01
3.02
3.13
0.98
1.00
1.01
1.02
1.01

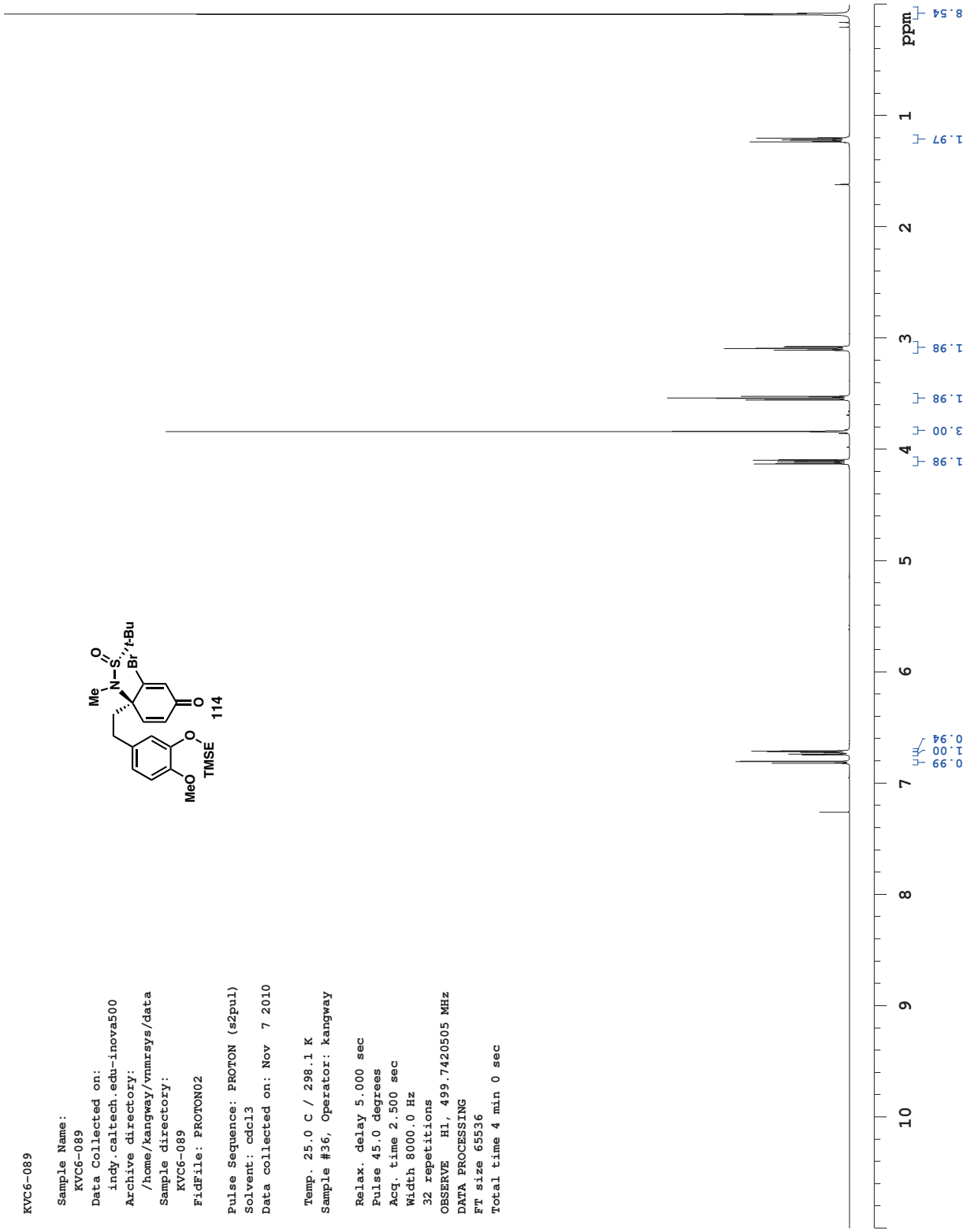

RN4-189
Cepharatine D
Sample Name:
RN4-189
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
RN4-189
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 2 2011
Temp. 25.0 C / 298.1 K
Sample #46, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2000 repetitions
OBSERVE C13, 125.6569623 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 8 min
OMe
MeO
Me N
HO
O
cepharatine D (123)
200
180
160
140
120
100
80
60
40
20
ppm

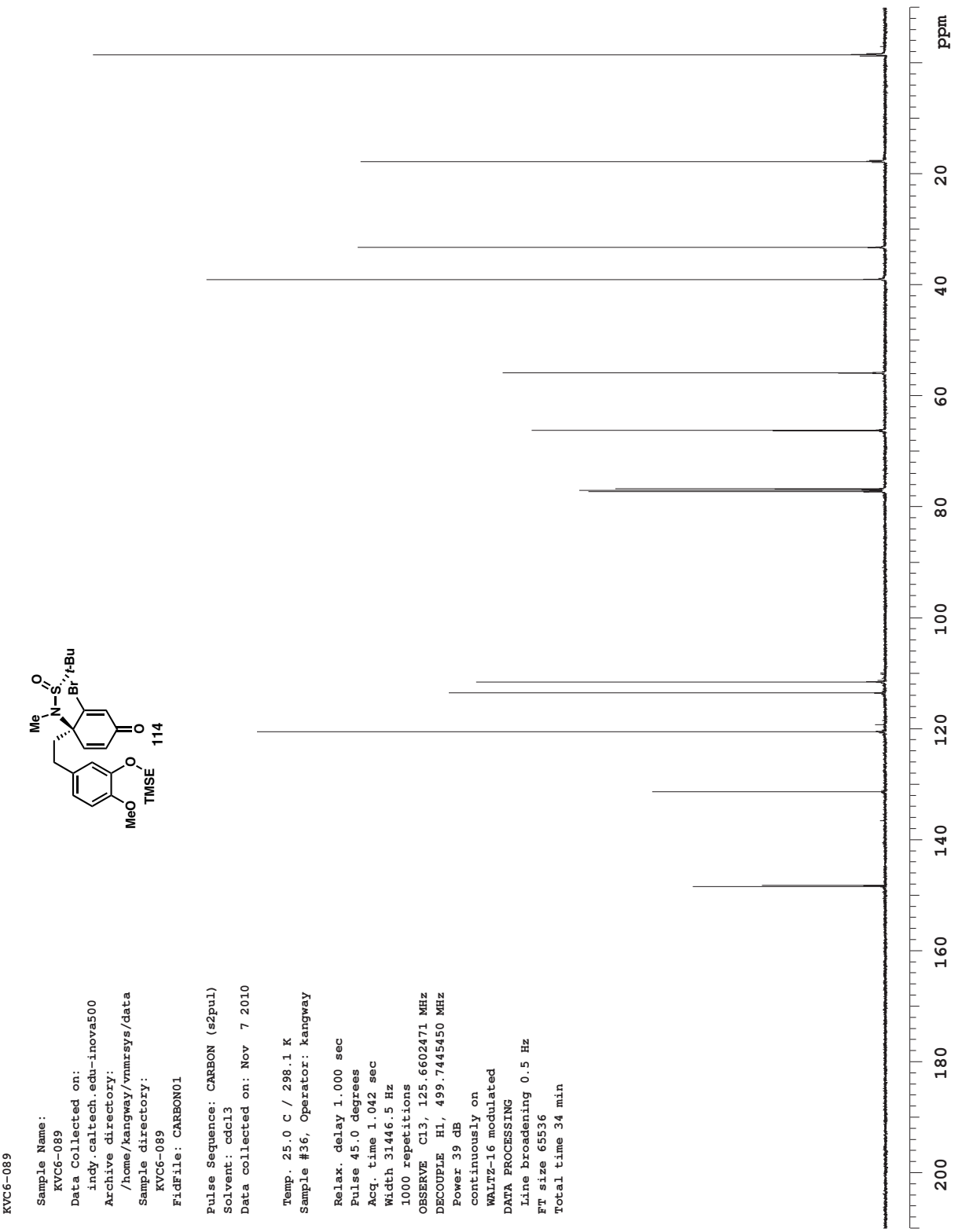

RN4-127
Sample Name:
RN4-127
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
RN4-127
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 20 2011
Temp. 25.0 C / 298.1 K
Sample #42, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290200 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
OMe
MeO
N
Me
O
O
120
ppm
1.00
1.00
1.01
1.05
2.90
2.98
1.08
3.29
1.12
3.09
1.01
2.05
1.08
1.04

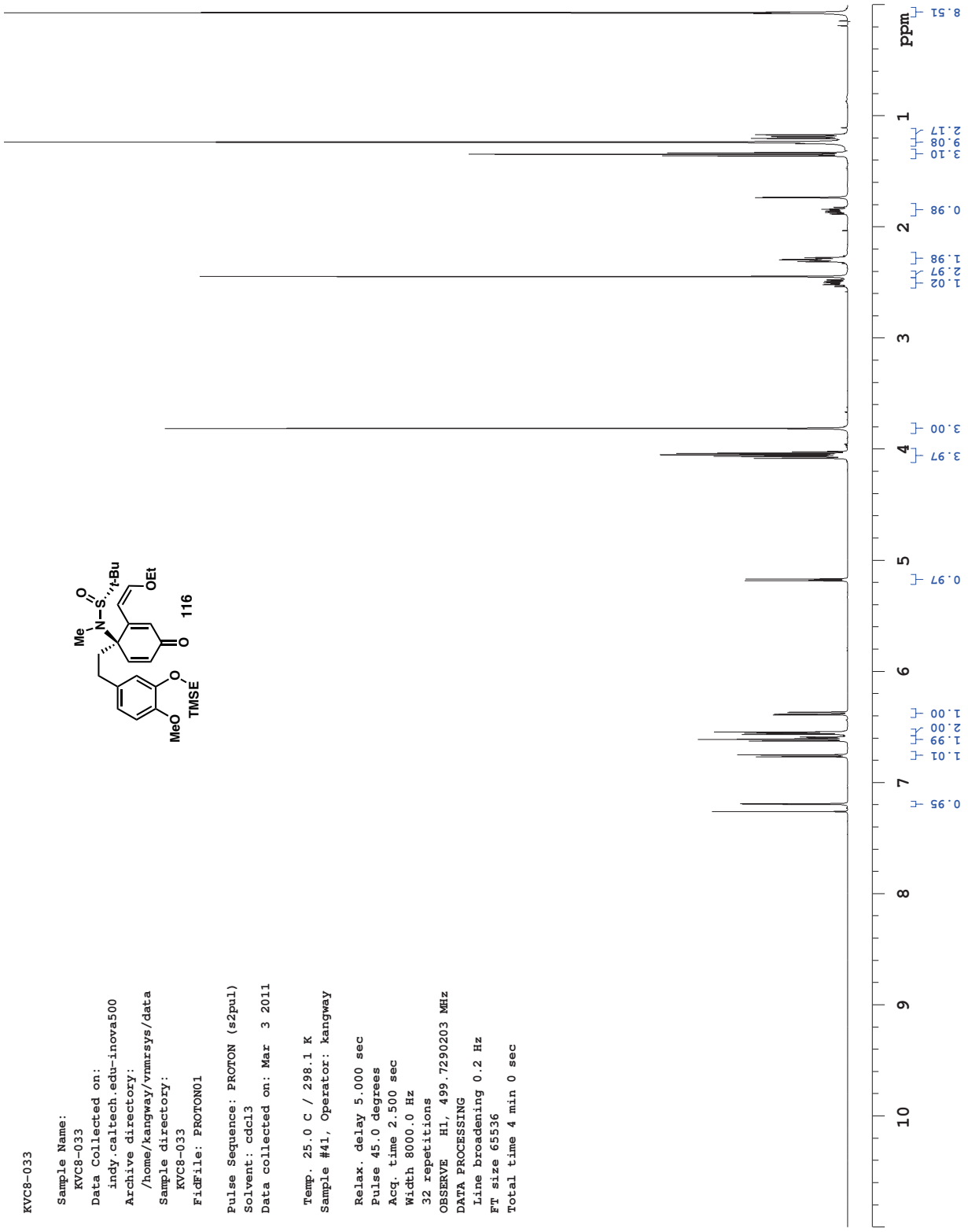

RN4-127
Sample Name:
RN4-127
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
RN4-127
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 20 2011
Temp. 25.0 C / 298.1 K
Sample #42, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6569642 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
OMe
MeO
N
Me
O
O
120
200
180
160
140
120
100
80
60
40
20
ppm

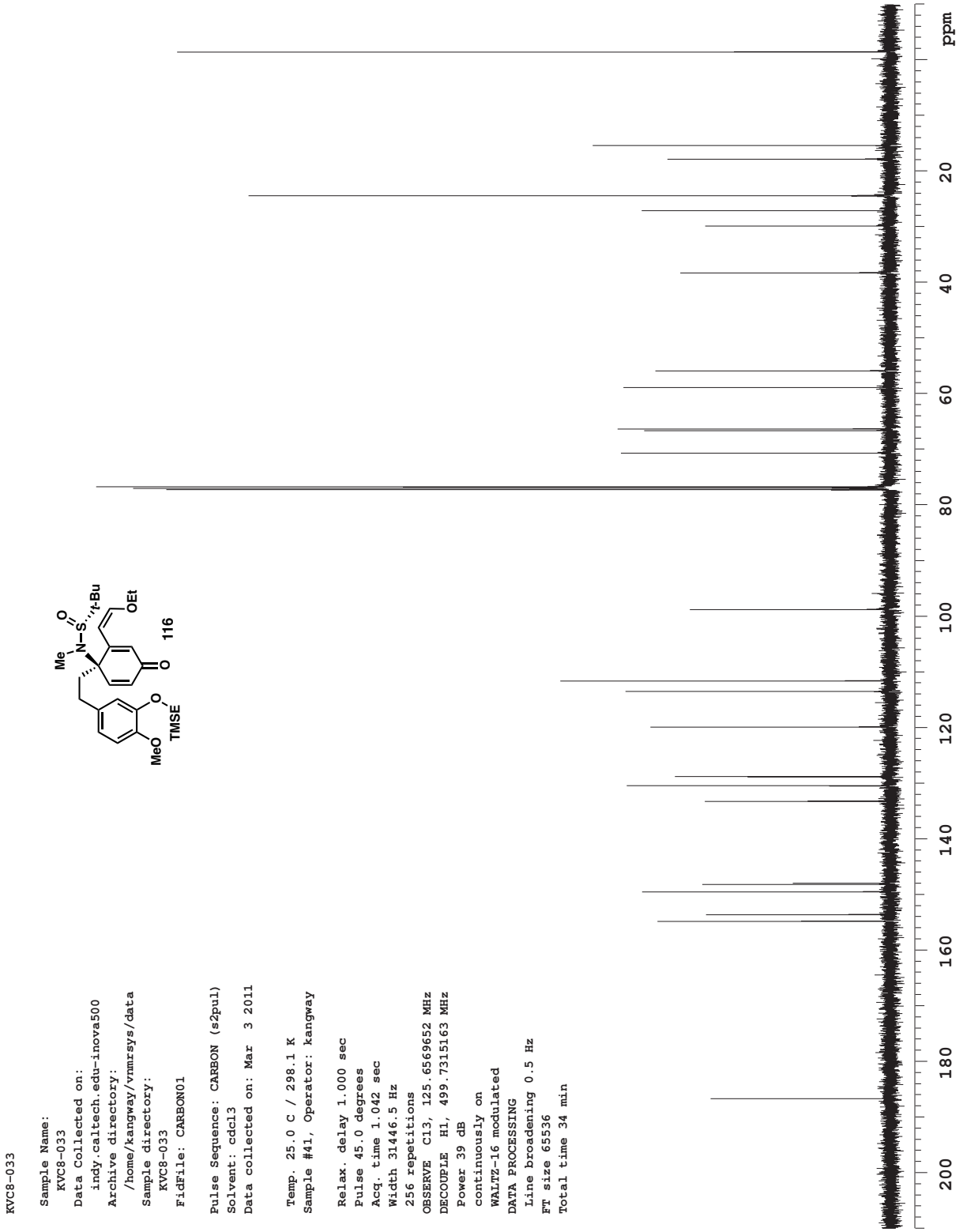

RN4-142
Sample Name:
RN4-142
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
RN4-142
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 3 2011
Temp. 25.0 C / 298.1 K
Sample #33, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290203 MHz
DATA PROCESSING
FT size 65536
Total time 4 min 0 sec
OMe
MeO
OMe
O
N
Me
8-demethoxyrunanine (2)
ppm
1.11
2.05
1.09
4.03
1.05
1.00
2.03
0.99
3.03
3.07
3.05
0.97
1.00
0.99

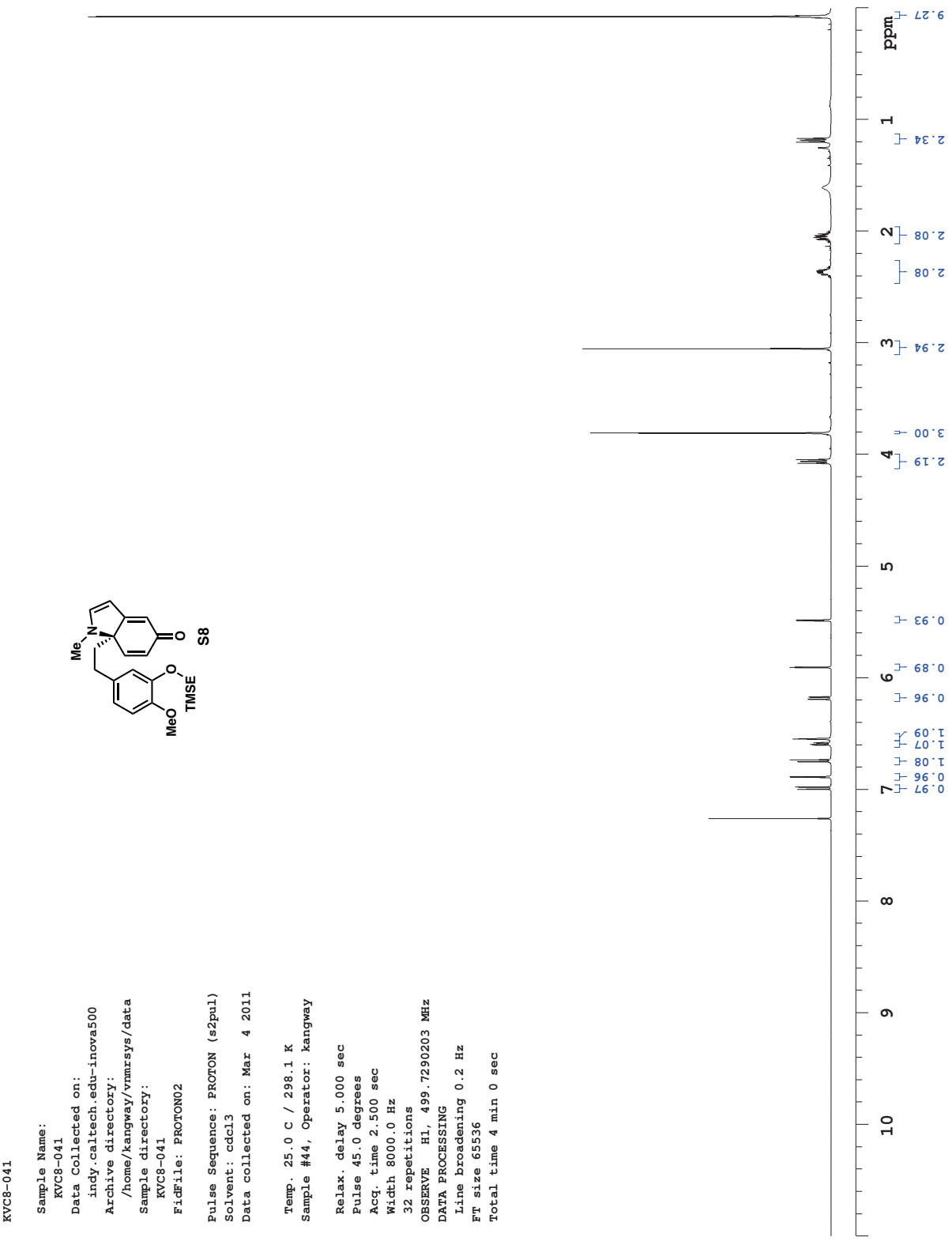

RN4-142
Sample Name:
RN4-142
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
RN4-142
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 3 2011
Temp. 25.0 C / 298.1 K
Sample #33, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6569652 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
OMe
MeO
N
Me
OMe
O
8-demethoxyrunanine (2)
200
180
160
140
120
100
80
60
40
20
ppm

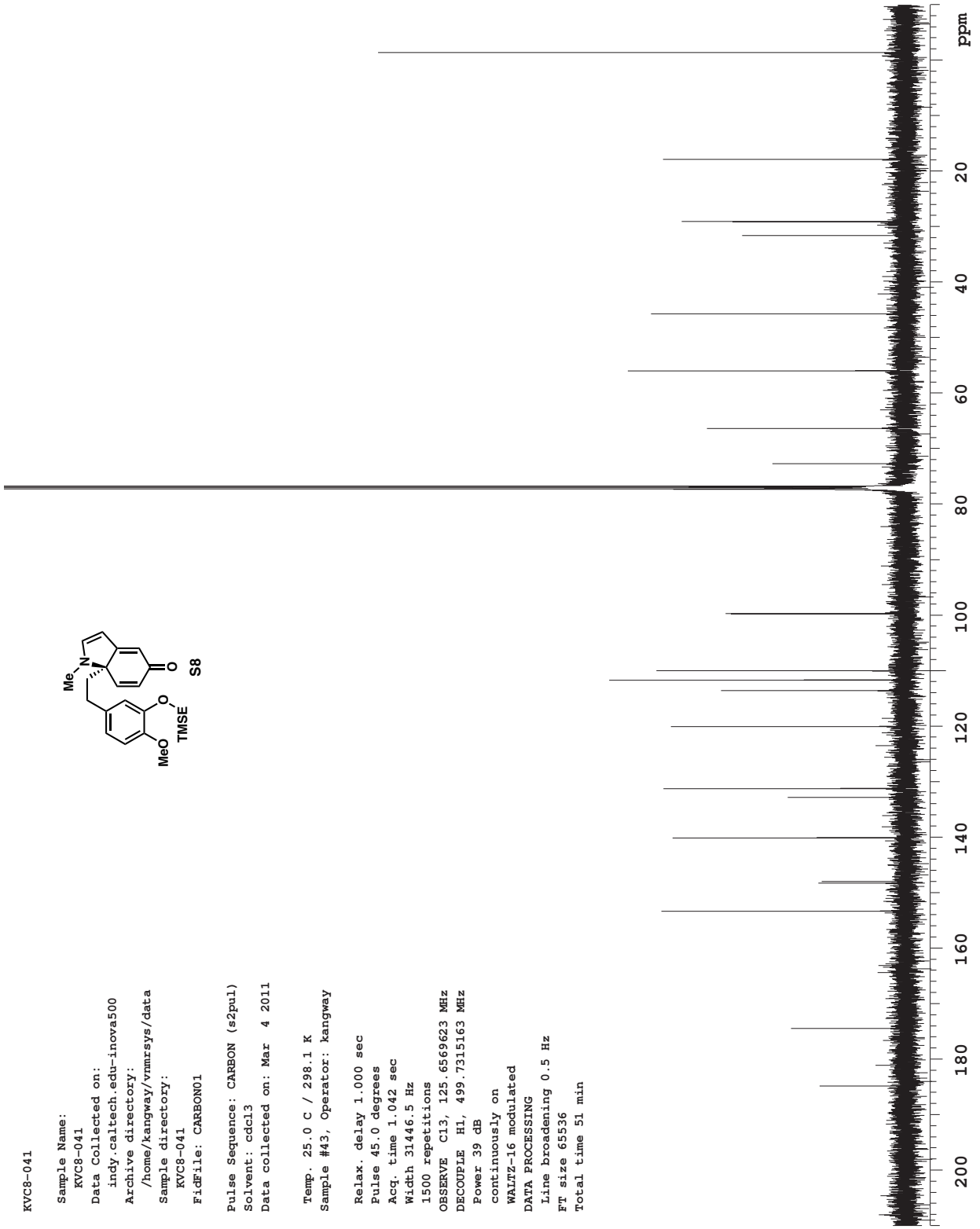

KVC6-089
Sample Name:
KVC6-089
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC6-089
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Nov 7 2010
Temp. 25.0 C / 298.1 K
Sample #36, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7420505 MHz
DATA PROCESSING
FT size 65536
Total time 4 min 0 sec
Me
O
N
S
Br
t-Bu
O
O
MeO
O
TMSE
114
ppm
10
9
8
7
6
5
4
3
2
1
8.54
1.97
1.98
1.98
3.00
1.98
0.99
1.00
0.94

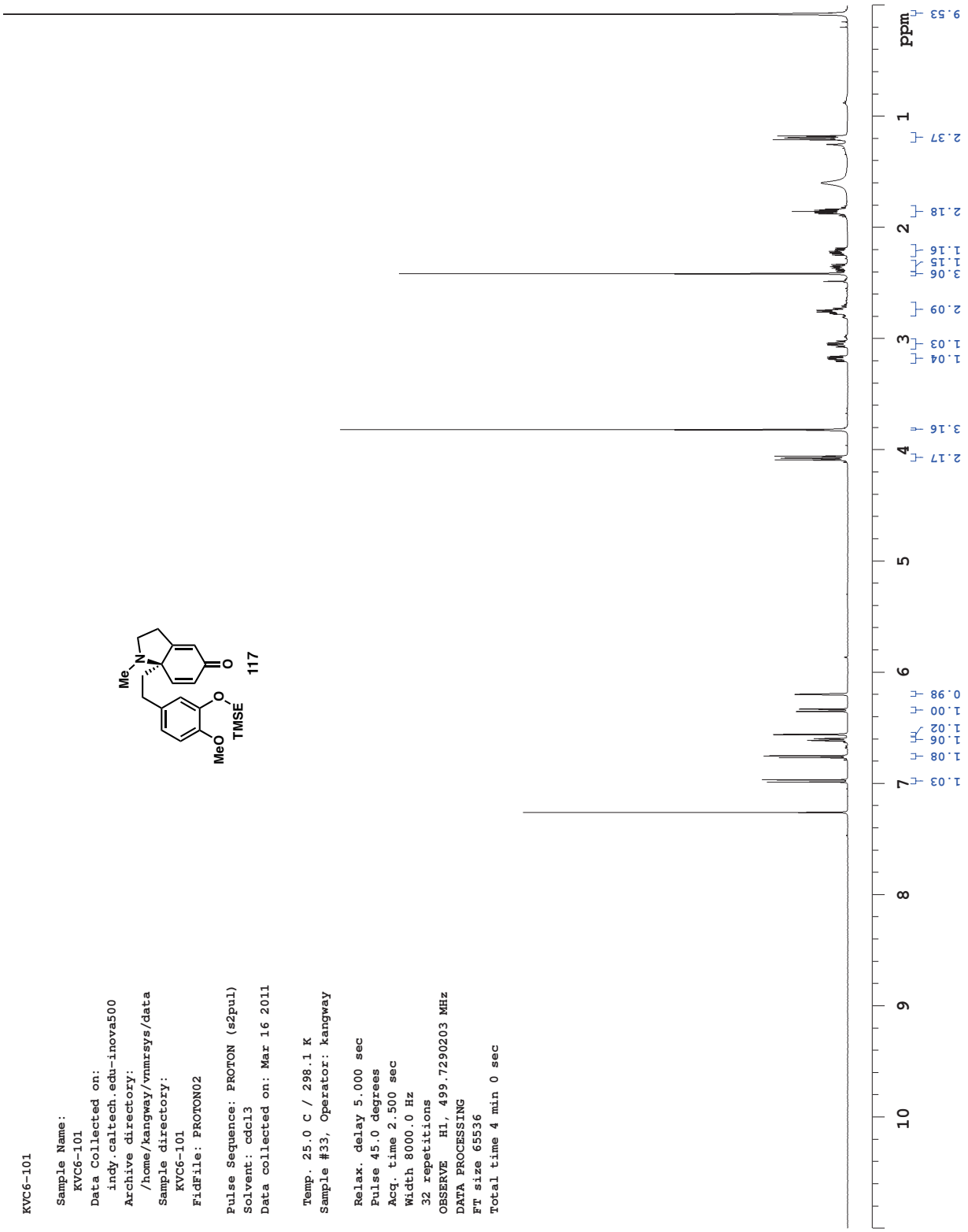

KVC6-089
Sample Name:
KVC6-089
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC6-089
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Nov 7 2010
Temp. 25.0 C / 298.1 K
Sample #36, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6602471 MHz
DECOUPLE H1, 499.7445450 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
Me
O
N
S
t-Bu
Br
O
MeO
O
TMSE
114
200
180
160
140
120
100
80
60
40
20
ppm

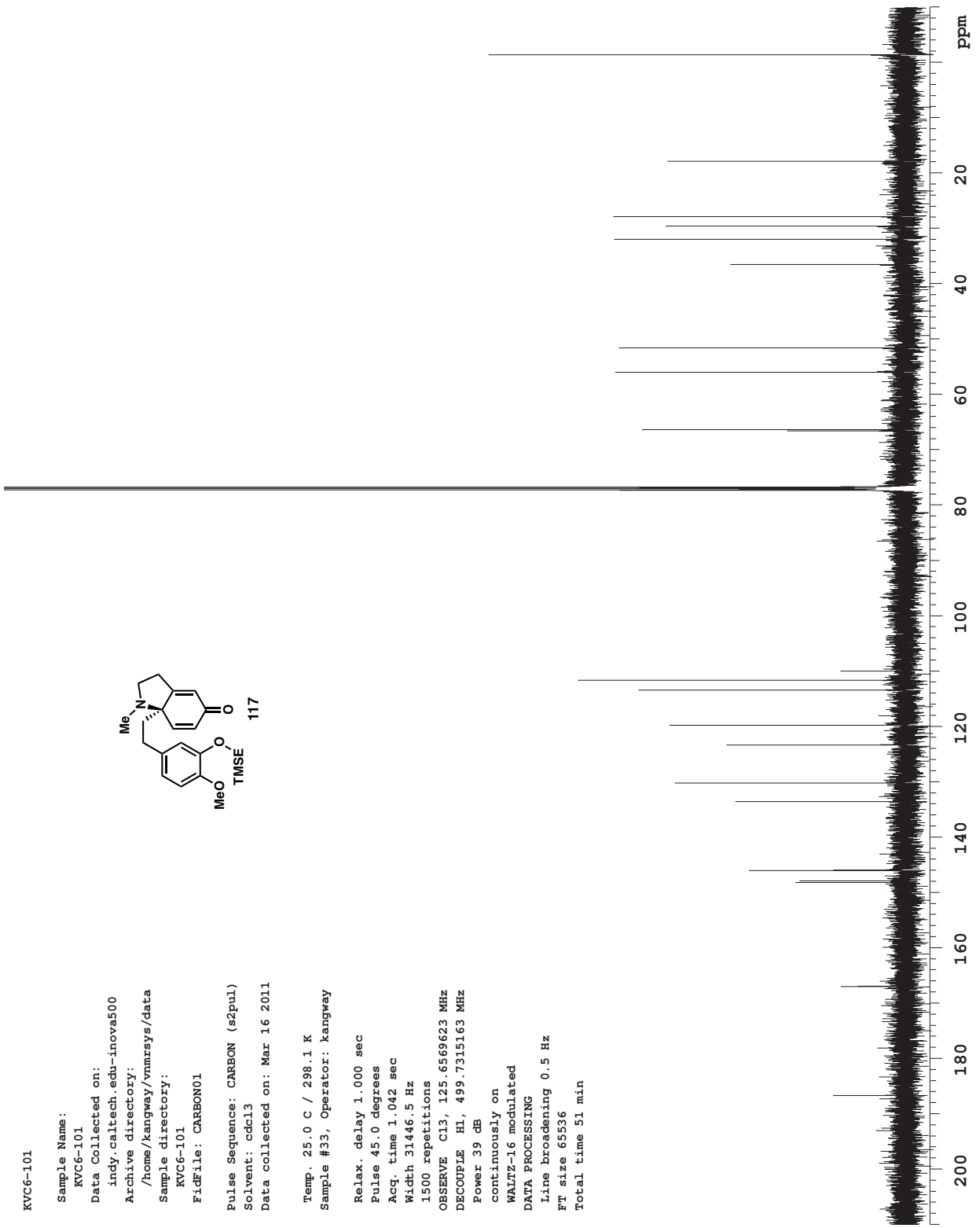

KVC8-033
Sample Name:
KVC8-033
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC8-033
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 3 2011
Temp. 25.0 C / 298.1 K
Sample #41, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290203 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Me
N
S
t-Bu
OEt
116
MeO
TMSE
ppm
8.51
3.10
9.08
2.17
0.98
1.98
2.97
1.02
3.00
3.97
0.97
1.00
2.00
1.99
1.01
0.95

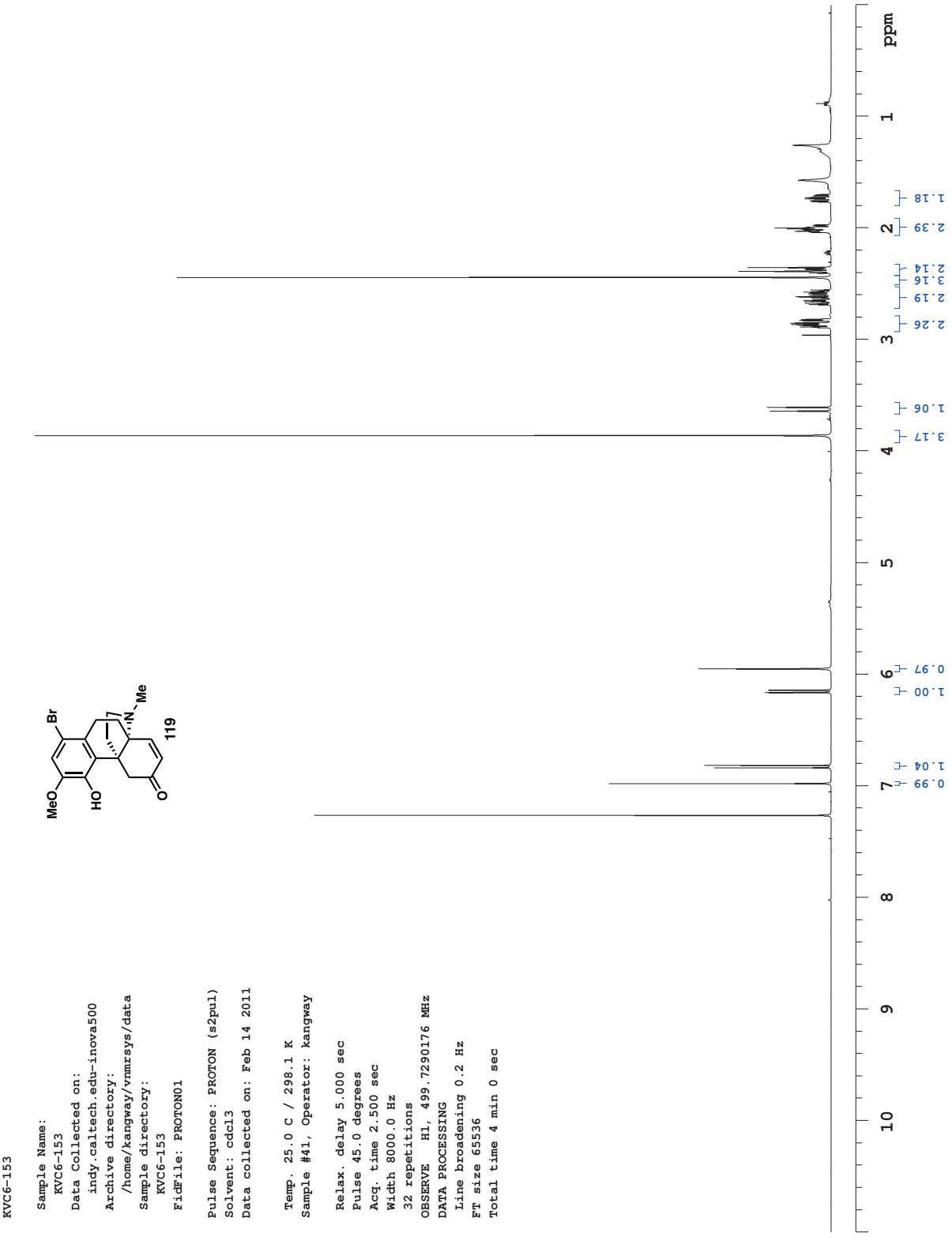

KVC8-033
Sample Name:
KVC8-033
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC8-033
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 3 2011
Temp. 25.0 C / 298.1 K
Sample #41, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
256 repetitions
OBSERVE C13, 125.6569652 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
Me
N
S
O
t-Bu
OEt
O
MeO
O
TMSE
116
200
180
160
140
120
100
80
60
40
20
ppm


KVC8-041
Sample Name:
KVC8-041
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC8-041
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 4 2011
Temp. 25.0 C / 298.1 K
Sample #44, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290203 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Me
N
O
O
TMSE
MeO
S8
ppm
9.27
2.34
2.08
2.08
2.94
3.00
2.19
0.93
0.89
0.96
1.09
1.07
1.08
0.96
0.97

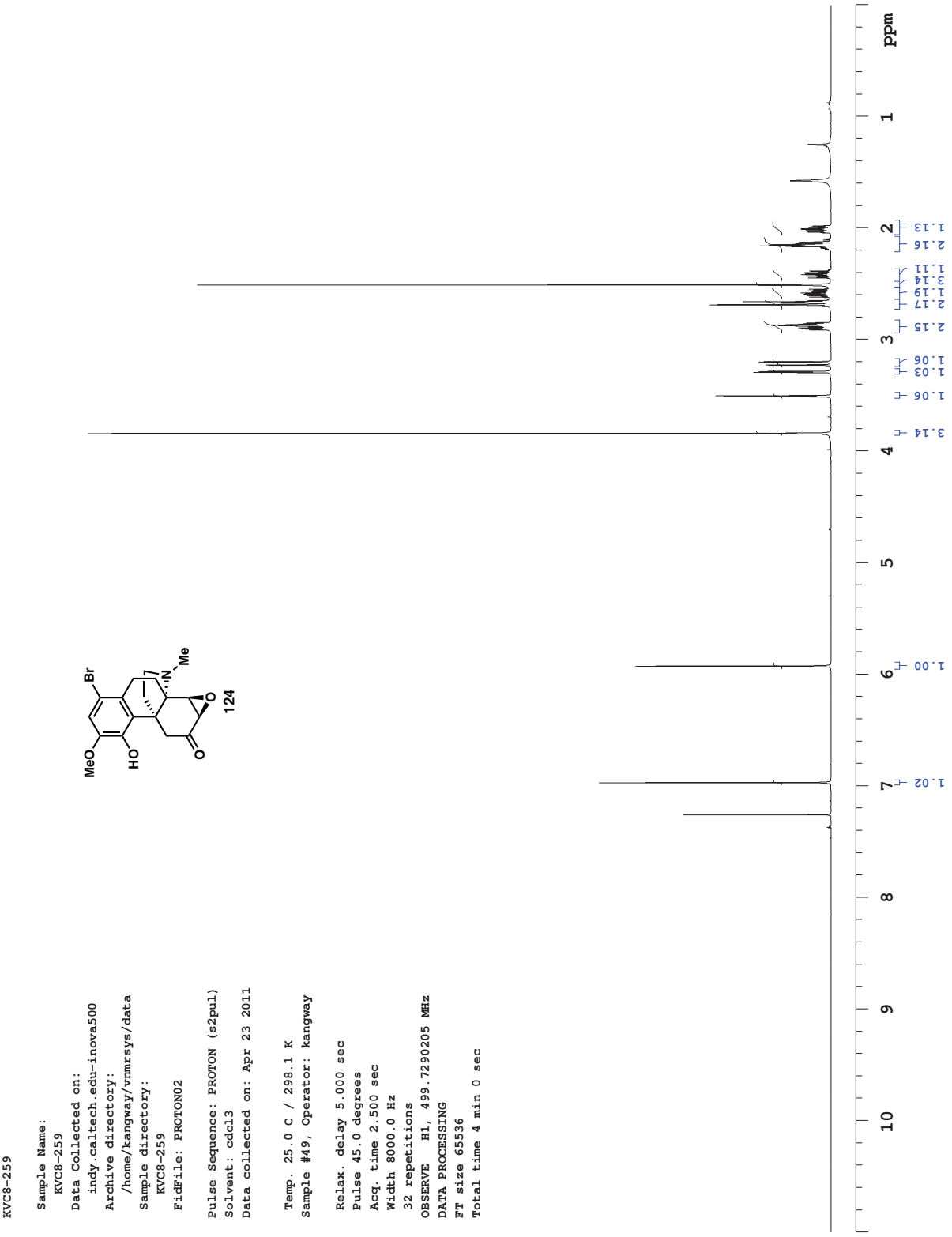

KVC8-041
Sample Name:
KVC8-041
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC8-041
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 4 2011
Temp. 25.0 C / 298.1 K
Sample #43, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6569623 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
Me
N
O
O
TMSE
MeO
S8
200
180
160
140
120
100
80
60
40
20
ppm

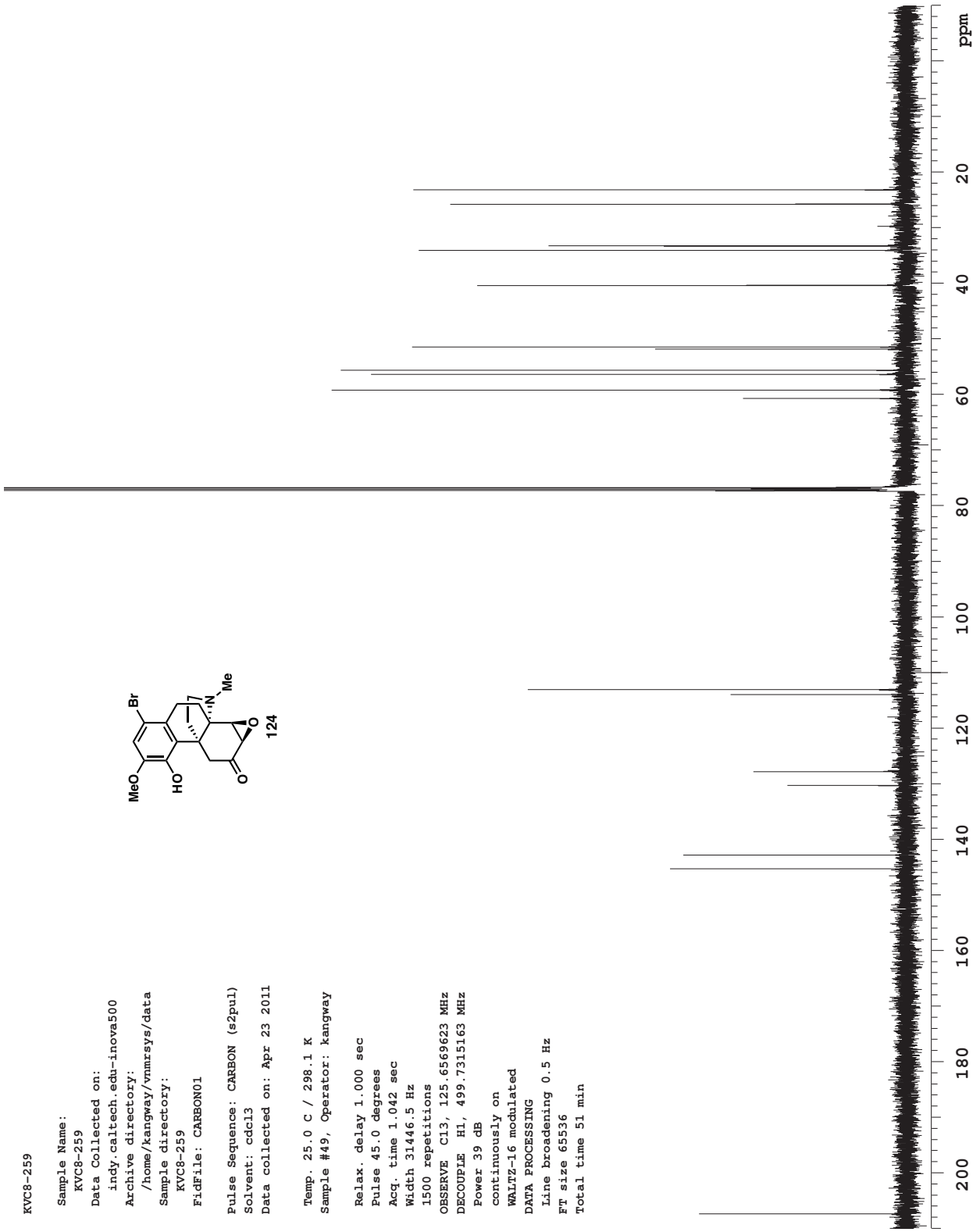

KVC6-101
Sample Name:
KVC6-101
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC6-101
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 16 2011
Temp. 25.0 C / 298.1 K
Sample #33, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290203 MHz
DATA PROCESSING
FT size 65536
Total time 4 min 0 sec
Me
N
O
O
TMSE
MeO
117
ppm
9.53
2.37
2.18
1.16
1.15
3.06
2.09
1.03
1.04
3.16
2.17
0.98
1.00
1.02
1.06
1.08
1.03

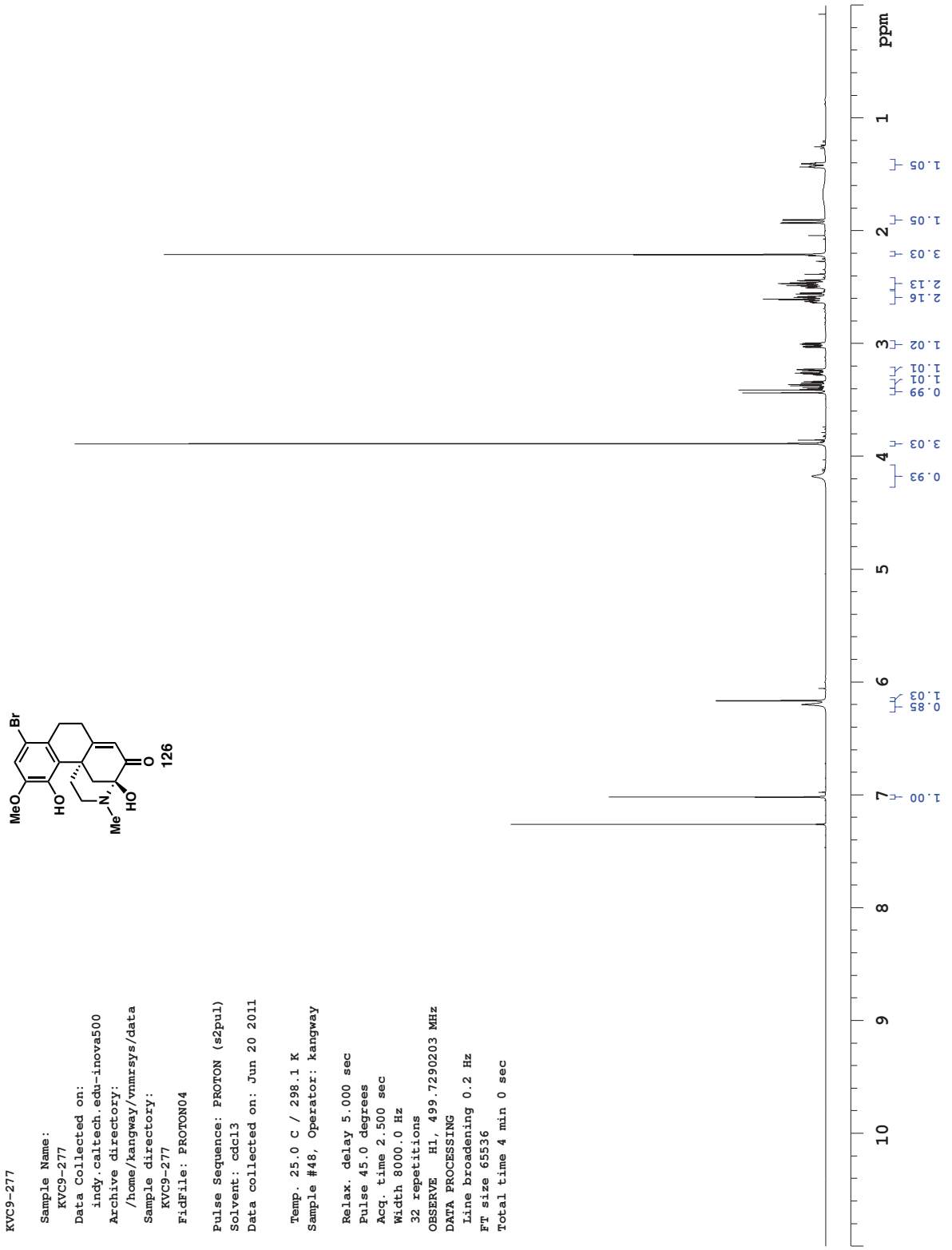

KVC6-101
Sample Name:
KVC6-101
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC6-101
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 16 2011
Temp. 25.0 C / 298.1 K
Sample #33, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6569623 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
Me
N
O
MeO
O
TMSE
117
200
180
160
140
120
100
80
60
40
20
ppm

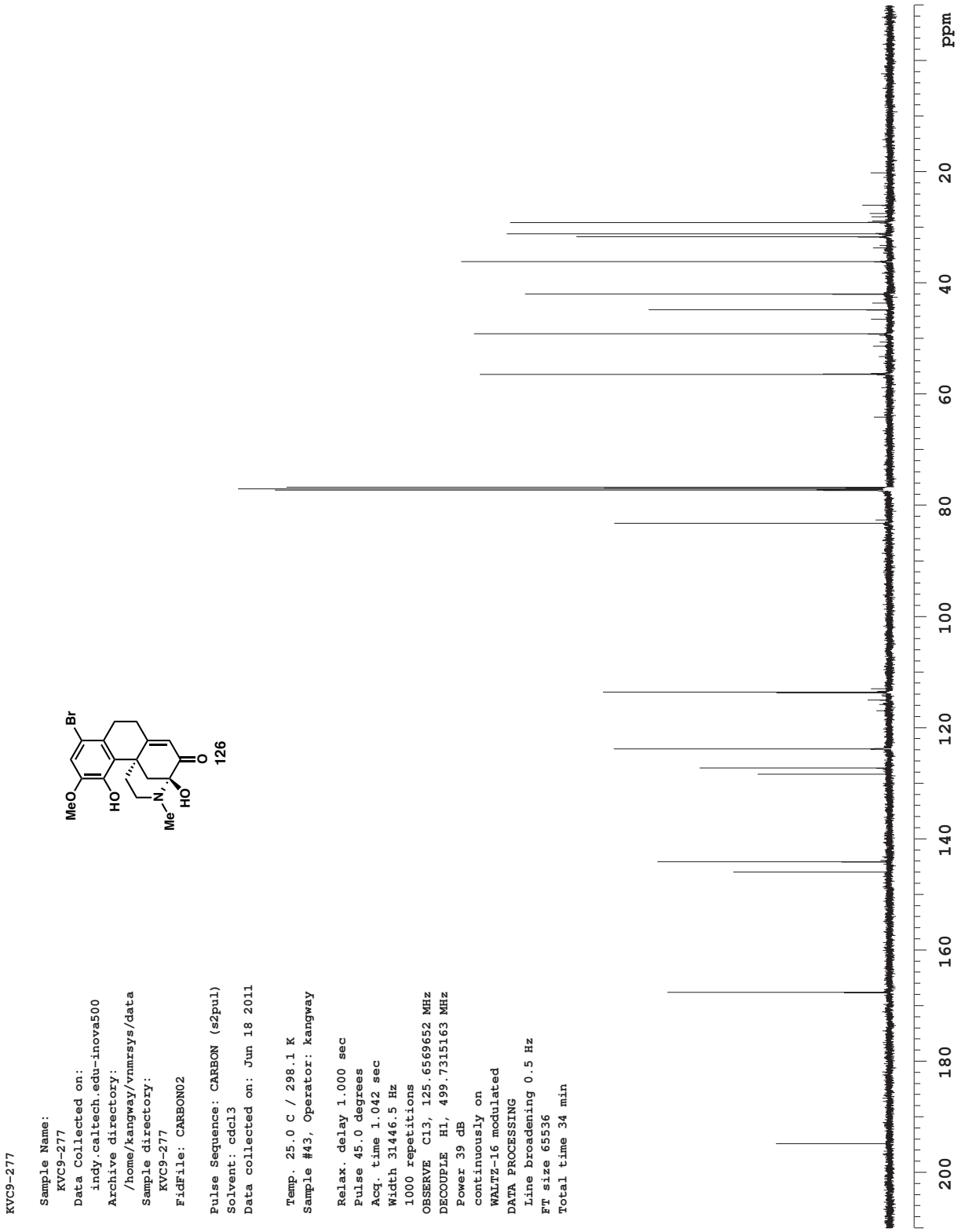

KVC6-153
Sample Name:
KVC6-153
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC6-153
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Feb 14 2011
Temp. 25.0 C / 298.1 K
Sample #41, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290176 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Br
MeO
HO
N
Me
O
119
ppm
1.18
2.39
2.14
3.16
2.19
2.26
1.06
3.17
0.97
1.00
1.04
0.99

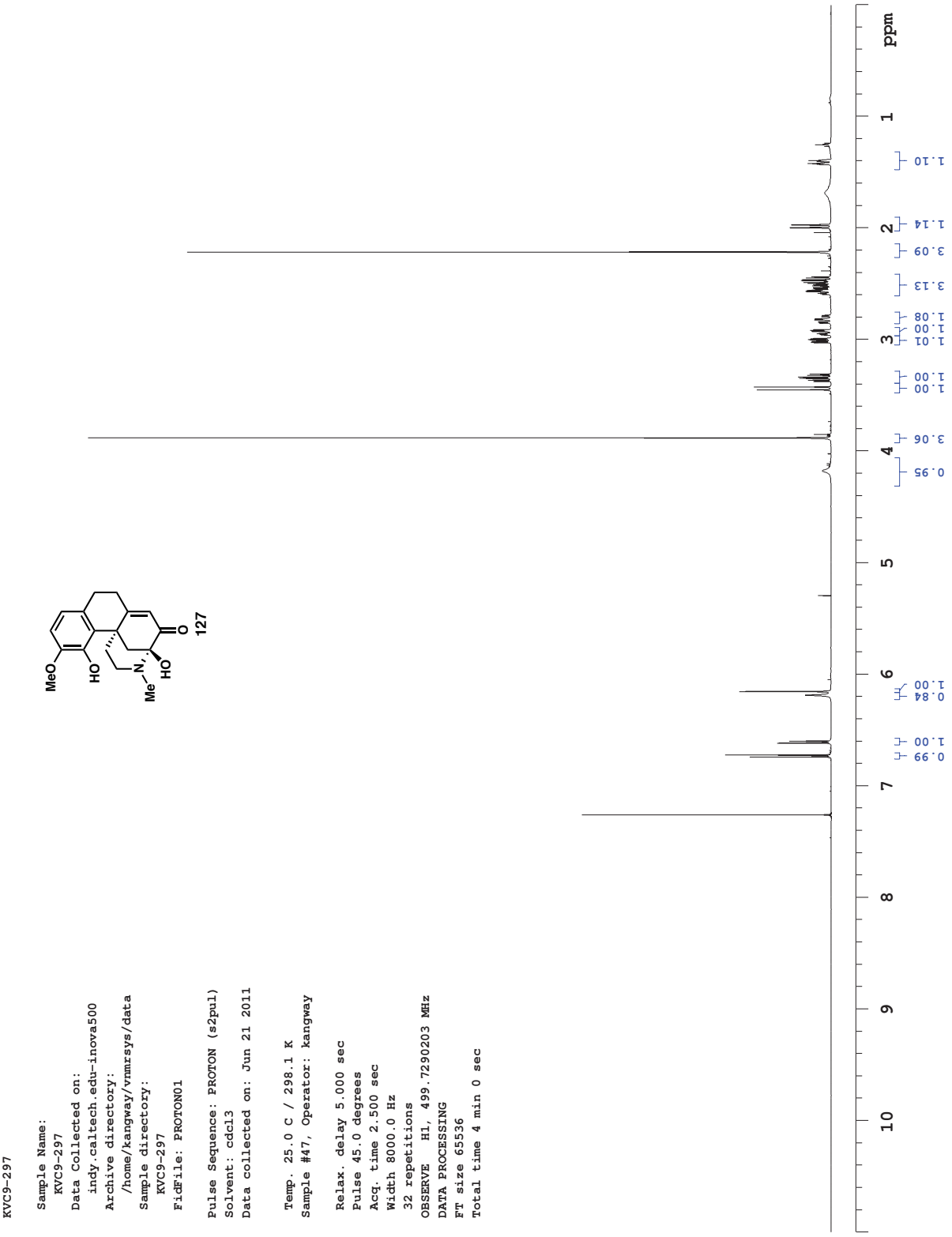
KVC6-153
Sample Name:
KVC6-153
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC6-153
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Feb 14 2011
Temp. 25.0 C / 298.1 K
Sample #41, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6569623 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
MeO
Br
HO
N
Me
O
119
200
180
160
140
120
100
80
60
40
20
ppm

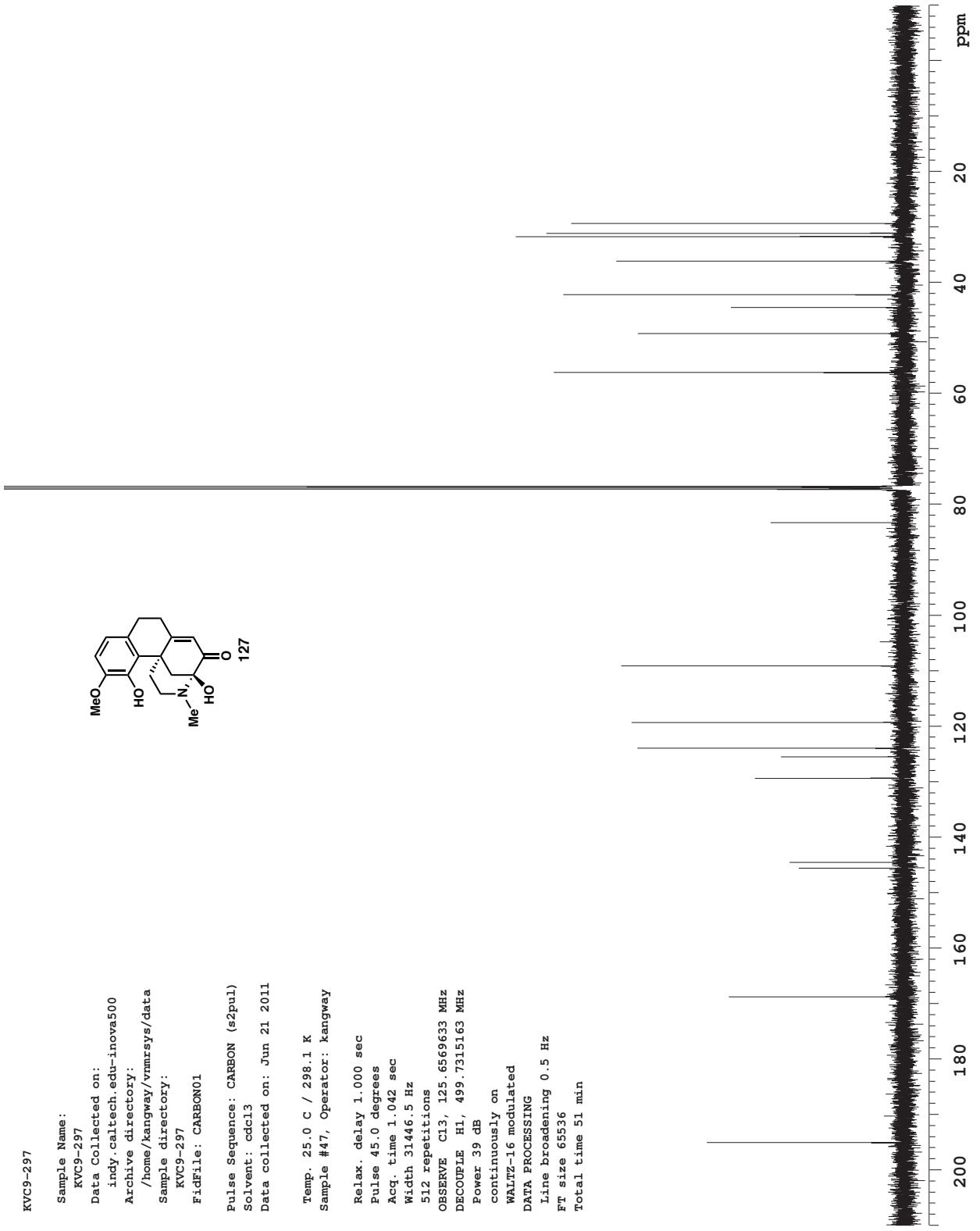

KVC8-259
Sample Name:
KVC8-259
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC8-259
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 23 2011
Temp. 25.0 C / 298.1 K
Sample #49, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290205 MHz
DATA PROCESSING
FT size 65536
Total time 4 min 0 sec
Br
Me
N
MeO
HO
O
O
124
ppm
10
9
8
7
6
5
4
3
2
1
1.00
1.02
3.14
1.06
1.03
1.06
2.15
2.17
1.19
3.14
1.11
2.16
1.13

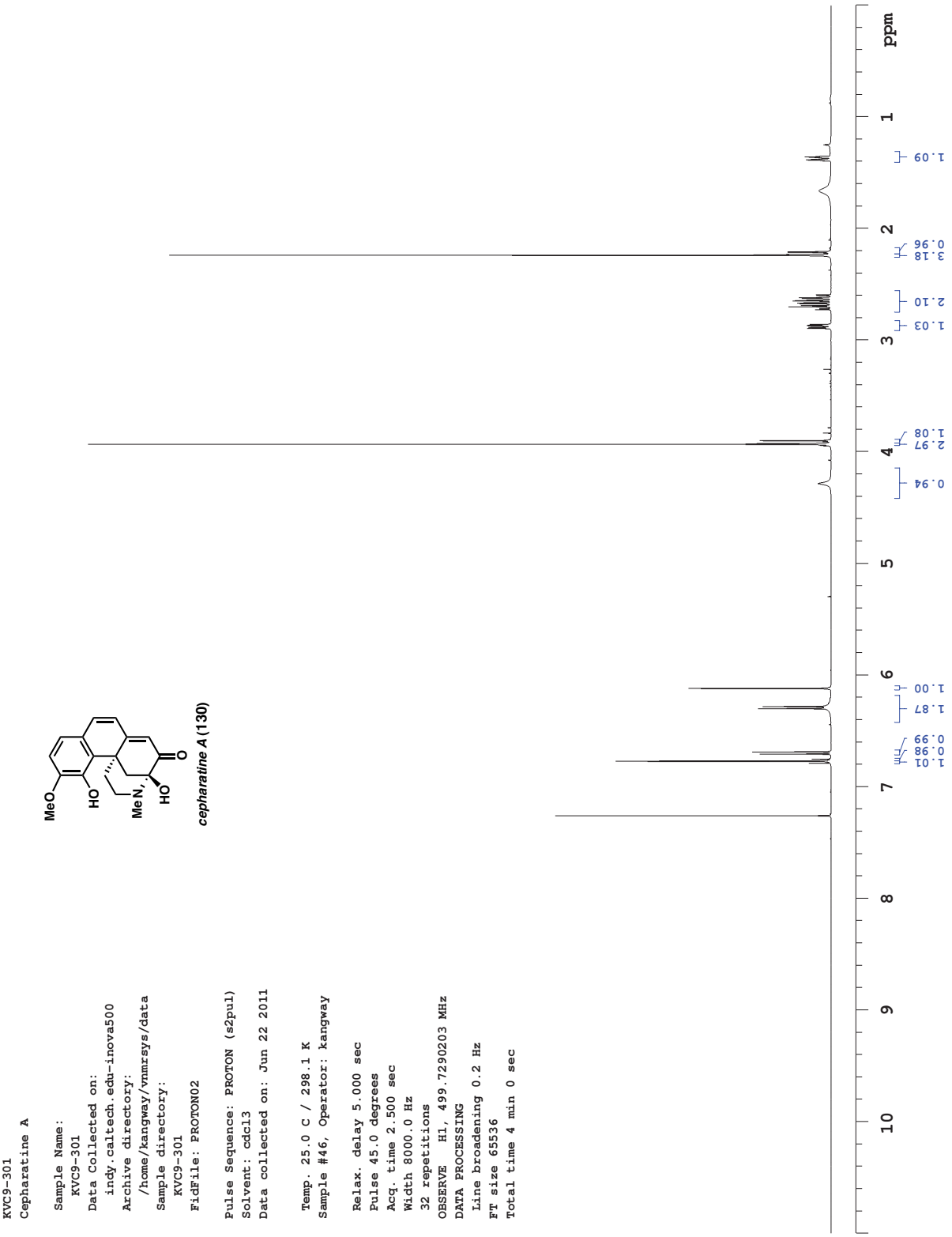

KVC8-259
Sample Name:
KVC8-259
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC8-259
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 23 2011
Temp. 25.0 C / 298.1 K
Sample #49, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6569623 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
Br
Me
N
O
MeO
HO
O
124
200
180
160
140
120
100
80
60
40
20
ppm

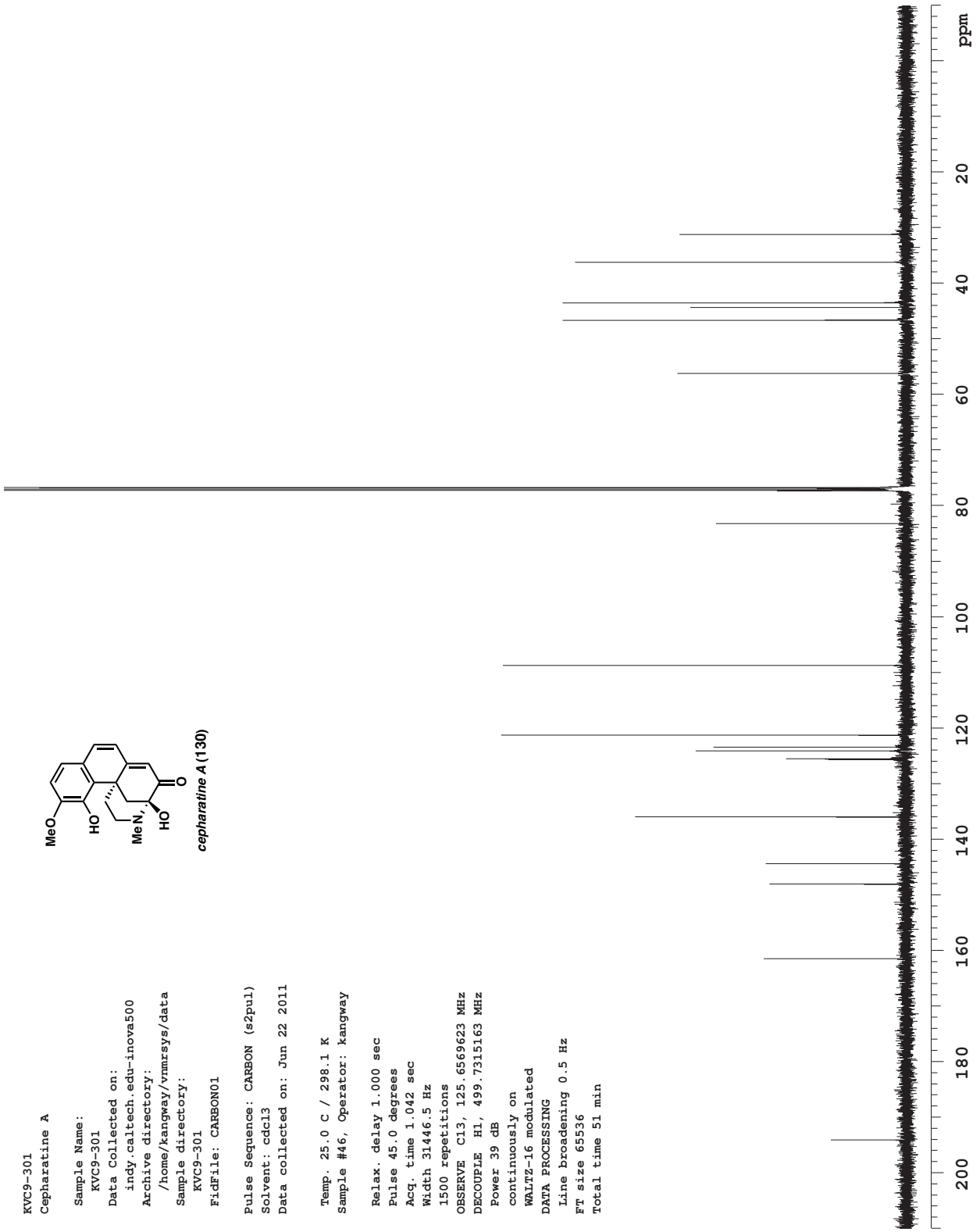

KVC9-277
Sample Name:
KVC9-277
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC9-277
FidFile: PROTON04
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 20 2011
Temp. 25.0 C / 298.1 K
Sample #48, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290203 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Br
MeO
HO
HO
Me
N
O
126
ppm
1.00
0.85
1.03
0.93
3.03
0.99
1.01
1.01
1.02
3.03
2.16
2.13
1.05
1.05

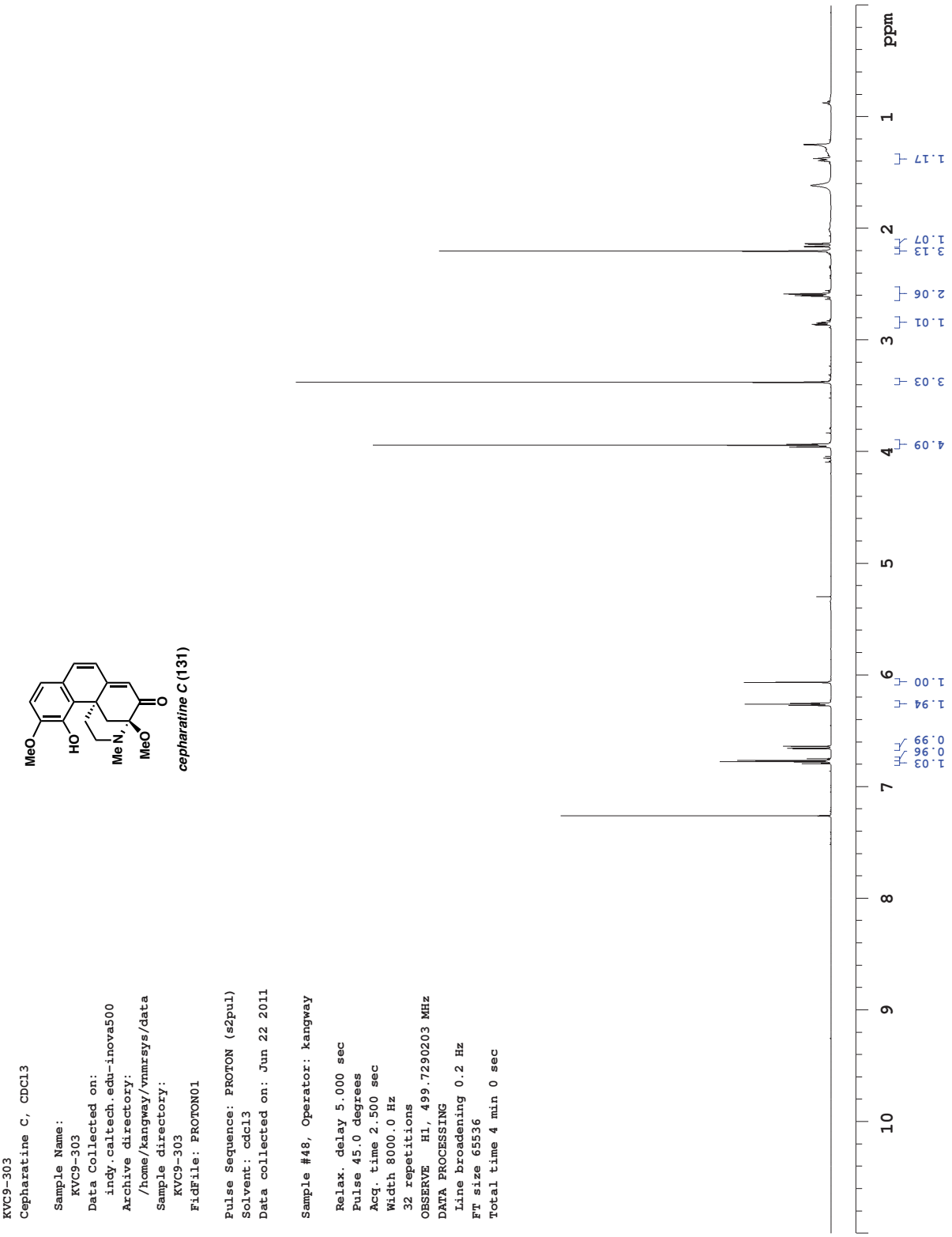

KVC9-277
Sample Name:
KVC9-277
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC9-277
FidFile: CARBON02
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 18 2011
Temp. 25.0 C / 298.1 K
Sample #43, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6569652 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
Br
MeO
HO
N
Me
HO
O
126
200
180
160
140
120
100
80
60
40
20
ppm

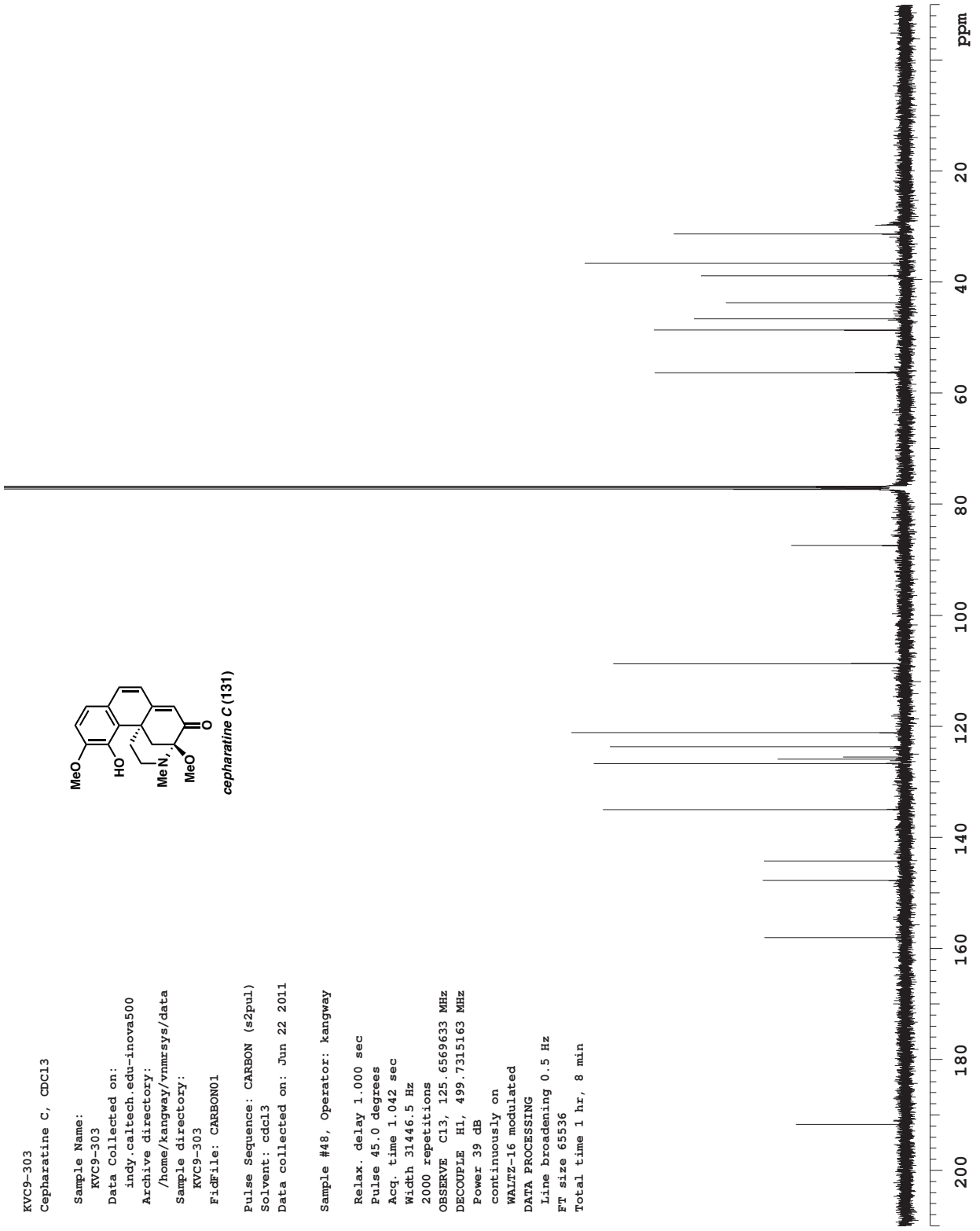

KVC9-297
Sample Name:
KVC9-297
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC9-297
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 21 2011
Temp. 25.0 C / 298.1 K
Sample #47, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290203 MHz
DATA PROCESSING
FT size 65536
Total time 4 min 0 sec
MeO
HO
Me
N
HO
O
127
ppm
1.10
1.14
3.09
3.13
1.08
1.00
1.01
1.00
1.00
3.06
0.95
0.84
1.00
0.99
1.00

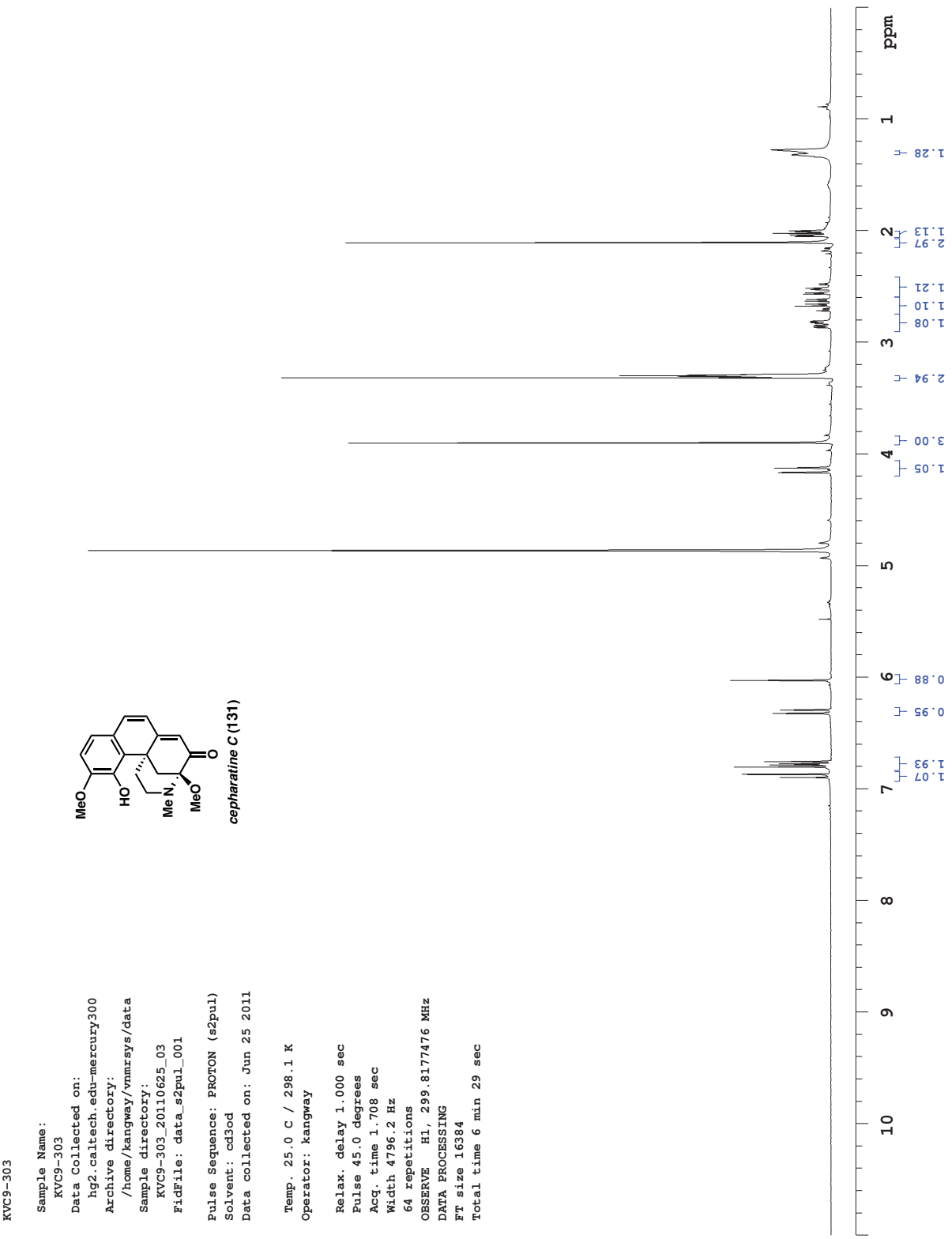

KVC9-297
Sample Name:
KVC9-297
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC9-297
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 21 2011
Temp. 25.0 C / 298.1 K
Sample #47, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6569633 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
MeO
HO
N
Me
HO
O
127
200
180
160
140
120
100
80
60
40
20
ppm


KVC9-301
Cepharatine A
Sample Name:
KVC9-301
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC9-301
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 22 2011
Temp. 25.0 C / 298.1 K
Sample #46, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290203 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
MeO
HO
Me N
HO
O
cepharatine A (130)
ppm
10
9
8
7
6
5
4
3
2
1
1.09
3.18
0.96
2.10
1.03
2.97
1.08
0.94
1.00
1.87
1.01
0.98
0.99


KVC9-301
Cepharatine A
Sample Name:
KVC9-301
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC9-301
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 22 2011
Temp. 25.0 C / 298.1 K
Sample #46, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6569623 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
MeO
HO
Me N
HO
O
cepharatine A (130)
200
180
160
140
120
100
80
60
40
20
ppm


KVC9-303
Cepharatine C, CDCl3
Sample Name:
KVC9-303
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC9-303
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 22 2011
Sample #48, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290203 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
MeO
HO
Me N
MeO
O
cepharatine C (131)
ppm
1.17
3.13
1.07
2.06
1.01
3.03
4.09
1.00
1.94
1.03
0.96
0.99


KVC9-303
Cepharatine C, CDCl3
Sample Name:
KVC9-303
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC9-303
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 22 2011
Sample #48, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2000 repetitions
OBSERVE C13, 125.6569633 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 8 min
MeO
HO
Me N
MeO
O
cepharatine C (131)
200
180
160
140
120
100
80
60
40
20
ppm


KVC9-303
Sample Name:
KVC9-303
Data Collected on:
hg2.caltech.edu-mercury300
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC9-303_20110625_03
FidFile: data_s2pul_001
Pulse Sequence: PROTON (s2pul)
Solvent: cd3od
Data collected on: Jun 25 2011
Temp. 25.0 C / 298.1 K
Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.708 sec
Width 4796.2 Hz
64 repetitions
OBSERVE H1, 299.8177476 MHz
DATA PROCESSING
FT size 16384
Total time 6 min 29 sec
MeO
HO
Me N
MeO
O
cepharatine C (131)
ppm
1.28
2.97
1.13
1.21
1.10
1.08
2.94
3.00
1.05
0.88
0.95
1.07
1.93

KVC9-303
Cepharatine C, methanol-d4
Sample Name:
KVC9-303
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC9-303
FidFile: CARBON02
Pulse Sequence: CARBON (s2pul)
Solvent: cd3od
Data collected on: Jun 25 2011
Sample #20, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6572792 MHz
DECOUPLE H1, 499.7334852 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
MeO
HO
Me N
MeO
O
cepharatine C (131)
200
180
160
140
120
100
80
60
40
20
ppm

APPENDIX 2

X-Ray Crystallography Reports Relevant to Chapter 2:

Development of a Diastereoselective 1,2-Addition to Sulfinyl Imines[†]

[†] The work disclosed in this appendix for the X-ray crystallographic analysis of **97d** was completed entirely by Larry Henling and Dr. Michael Day in the Caltech X-ray crystallography lab.

A2.1 Crystal Structure analysis of sulfinamide 97d

Figure A2.1. Sulfinamide **97d**. Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition number 780836.

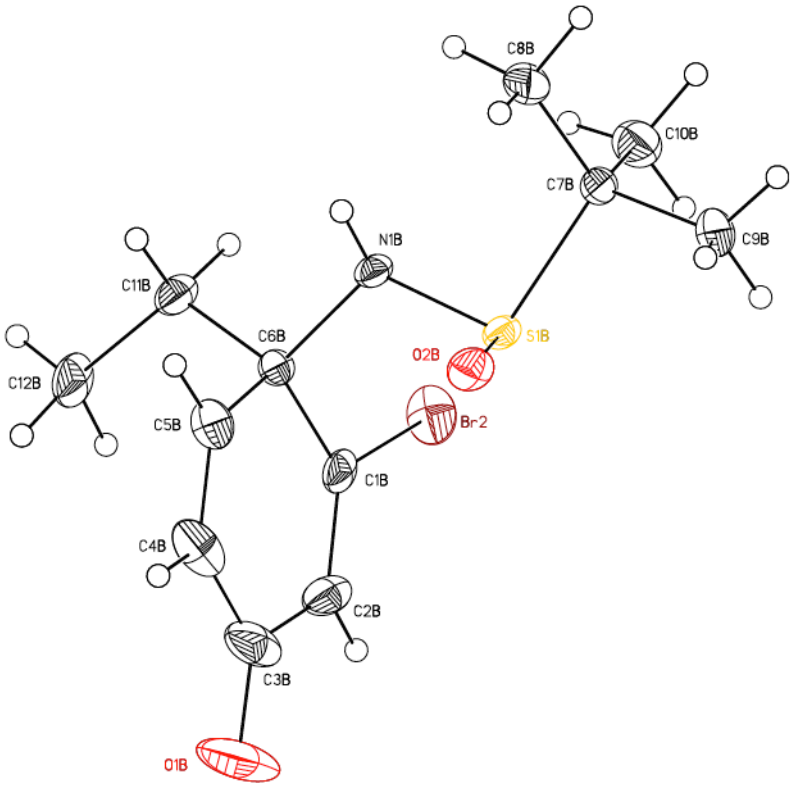
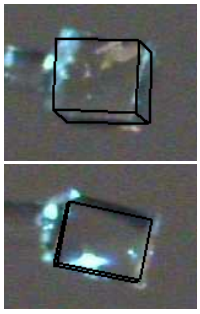


Table A2.1. Crystal data and structure refinement for sulfinamide **97d** (CCDC 780836).



Empirical formula	$C_{12}H_{18}BrNO_2S$
Formula weight	320.24
Crystallization Solvent	Benzene
Crystal Habit	Block
Crystal size	0.19 x 0.17 x 0.15 mm^3
Crystal color	Pale yellow

Data Collection

Type of diffractometer	Bruker KAPPA APEX II	
Wavelength	0.71073 Å MoKα	
Data Collection Temperature	100(2) K	
θ range for 9971 reflections used in lattice determination	2.36 to 28.59°	
Unit cell dimensions	a = 9.9624(4) Å b = 17.8137(8) Å c = 12.6175(6) Å	α= 90° β= 98.264(2)° γ = 90°
Volume	2215.94(17) $Å^3$	
Z	6	
Crystal system	Monoclinic	
Space group	$P2_1$	
Density (calculated)	1.440 Mg/m^3	
F(000)	984	
Data collection program	Bruker APEX2 v2009.7-0	
θ range for data collection	1.63 to 29.93°	
Completeness to θ = 29.93°	99.9 %	
Index ranges	$-13 \leq h \leq 13$, $-25 \leq k \leq 25$, $-17 \leq l \leq 17$	
Data collection scan type	ω scans; 9 settings	
Data reduction program	Bruker SAINT-Plus v7.66A	
Reflections collected	50720	
Independent reflections	12745 [R_{int}= 0.0422]	
Absorption coefficient	2.915 mm^{-1}	
Absorption correction	Gaussian	
Max. and min. transmission	0.7274 and 0.6375	

Table A2.1.(continued)

Structure solution and Refinement

Structure solution program	Bruker XS 2008/1
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Geometric positions
Structure refinement program	Bruker XL 2008/1
Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	12745 / 1 / 676
Treatment of hydrogen atoms	Riding
Goodness-of-fit on F^2	1.083
Final R indices [$I>2\sigma(I)$, 10731 reflections]	R1 = 0.0257, *w*R2 = 0.0308
R indices (all data)	R1 = 0.0344, *w*R2 = 0.0315
Type of weighting scheme used	Sigma
Weighting scheme used	$w=1/\sigma^2(Fo^2)$
Max shift/error	0.003
Average shift/error	0.000
Absolute structure determination	Anomalous differences
Absolute structure parameter	-0.011(2)
Largest diff. peak and hole	0.896 and -0.565 e.$Å^{-3}$

Special Refinement Details

Crystals were mounted on a glass fiber using Paratone oil then placed on the diffractometer under a nitrogen stream at 100K.

Refinement of F^2 against ALL reflections. The weighted R-factor (*w*R) and goodness of fit (S) are based on F^2, conventional R-factors (R) are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R-factors based on ALL data will be even larger.

All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Table A2.2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for RUN02 (CCDC 780836). U(eq) is defined as the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
Br(1)	826(1)	7627(1)	10809(1)	30(1)
S(1A)	290(1)	9531(1)	9058(1)	15(1)
O(1A)	4648(1)	8151(1)	8555(1)	29(1)
O(2A)	793(1)	10261(1)	8672(1)	20(1)
N(1A)	792(2)	9400(1)	10355(1)	16(1)
C(1A)	2103(2)	8250(1)	10247(2)	18(1)
C(2A)	2902(2)	7960(1)	9602(2)	21(1)
C(3A)	3913(2)	8416(1)	9154(2)	21(1)
C(4A)	3986(2)	9211(1)	9477(2)	21(1)
C(5A)	3198(2)	9493(1)	10137(2)	18(1)
C(6A)	2156(2)	9055(1)	10635(2)	15(1)
C(7A)	-1532(2)	9678(1)	9070(2)	17(1)
C(8A)	-1753(2)	10415(1)	9636(2)	22(1)
C(9A)	-2121(2)	9721(2)	7891(2)	31(1)
C(10A)	-2076(2)	9004(1)	9603(2)	28(1)
C(11A)	2518(2)	9089(1)	11865(2)	22(1)
C(12A)	3829(2)	8682(1)	12286(2)	27(1)
Br(2)	5571(1)	1465(1)	7107(1)	31(1)
S(1B)	2422(1)	501(1)	5939(1)	16(1)
O(1B)	1957(2)	3439(1)	5749(1)	58(1)
O(2B)	965(1)	639(1)	5519(1)	22(1)
N(1B)	2730(2)	670(1)	7254(1)	16(1)
C(1B)	3798(2)	1872(1)	6934(2)	19(1)
C(2B)	3526(2)	2495(1)	6370(2)	27(1)
C(3B)	2179(2)	2846(1)	6243(2)	36(1)
C(4B)	1137(2)	2458(1)	6737(2)	33(1)
C(5B)	1425(2)	1837(1)	7295(2)	24(1)
C(6B)	2796(2)	1481(1)	7539(1)	16(1)
C(7B)	2599(2)	-528(1)	5961(2)	19(1)
C(8B)	1628(2)	-877(1)	6636(2)	26(1)
C(9B)	2225(3)	-737(1)	4781(2)	35(1)
C(10B)	4062(2)	-713(1)	6359(2)	29(1)
C(11B)	3279(2)	1518(1)	8758(2)	21(1)
C(12B)	3509(2)	2312(1)	9194(2)	28(1)
Br(3)	2741(1)	7173(1)	5606(1)	35(1)
S(1C)	64(1)	6168(1)	7644(1)	17(1)
O(1C)	4996(2)	5914(1)	9071(1)	52(1)
O(2C)	-642(1)	5473(1)	7941(1)	22(1)
N(1C)	570(2)	6064(1)	6458(1)	17(1)
C(1C)	2956(2)	6399(1)	6656(1)	20(1)
C(2C)	3922(2)	6447(1)	7474(2)	25(1)
C(3C)	4149(2)	5852(1)	8278(2)	28(1)
C(4C)	3287(2)	5189(1)	8077(2)	25(1)
C(5C)	2288(2)	5153(1)	7278(2)	23(1)

C(6C)	1962(2)	5764(1)	6444(2)	17(1)
C(7C)	-1303(2)	6864(1)	7301(2)	19(1)
C(8C)	-2331(2)	6590(1)	6379(2)	26(1)
C(9C)	-1951(2)	6934(1)	8319(2)	28(1)
C(10C)	-630(2)	7594(1)	7045(2)	33(1)
C(11C)	1989(2)	5403(1)	5324(2)	26(1)
C(12C)	3403(2)	5133(2)	5166(2)	32(1)

Table A2.3. Bond lengths [Å] and angles [°] for RUN02 (CCDC 780836).

Br(1)-C(1A)	1.9001(18)	C(6B)-C(11B)	1.546(2)
S(1A)-O(2A)	1.4999(13)	C(7B)-C(10B)	1.508(3)
S(1A)-N(1A)	1.6576(17)	C(7B)-C(8B)	1.512(3)
S(1A)-C(7A)	1.8365(16)	C(7B)-C(9B)	1.528(3)
O(1A)-C(3A)	1.220(2)	C(8B)-H(8B1)	0.920(18)
N(1A)-C(6A)	1.486(2)	C(8B)-H(8B2)	0.917(17)
N(1A)-H(1A)	0.692(16)	C(8B)-H(8B3)	1.001(19)
C(1A)-C(2A)	1.323(3)	C(9B)-H(9B1)	0.965(19)
C(1A)-C(6A)	1.515(2)	C(9B)-H(9B2)	0.93(2)
C(2A)-C(3A)	1.469(3)	C(9B)-H(9B3)	0.872(19)
C(2A)-H(2A)	0.928(17)	C(10B)-H(10D)	0.902(19)
C(3A)-C(4A)	1.474(3)	C(10B)-H(10E)	0.94(2)
C(4A)-C(5A)	1.323(3)	C(10B)-H(10F)	0.96(2)
C(4A)-H(4A)	0.935(19)	C(11B)-C(12B)	1.523(3)
C(5A)-C(6A)	1.506(2)	C(11B)-H(11C)	0.871(18)
C(5A)-H(5A)	0.950(16)	C(11B)-H(11D)	1.093(17)
C(6A)-C(11A)	1.542(3)	C(12B)-H(12D)	1.02(2)
C(7A)-C(8A)	1.526(3)	C(12B)-H(12E)	0.889(16)
C(7A)-C(10A)	1.514(3)	C(12B)-H(12F)	0.99(2)
C(7A)-C(9A)	1.521(3)	Br(3)-C(1C)	1.9030(18)
C(8A)-H(8A1)	0.89(2)	S(1C)-O(2C)	1.4983(12)
C(8A)-H(8A2)	0.998(18)	S(1C)-N(1C)	1.6569(16)
C(8A)-H(8A3)	0.980(18)	S(1C)-C(7C)	1.8452(18)
C(9A)-H(9A1)	0.93(2)	O(1C)-C(3C)	1.218(2)
C(9A)-H(9A2)	0.95(2)	N(1C)-C(6C)	1.489(2)
C(9A)-H(9A3)	0.923(19)	N(1C)-H(1C)	0.876(17)
C(10A)-H(10A)	0.963(17)	C(1C)-C(2C)	1.308(2)
C(10A)-H(10B)	1.01(2)	C(1C)-C(6C)	1.503(2)
C(10A)-H(10C)	0.879(18)	C(2C)-C(3C)	1.462(3)
C(11A)-C(12A)	1.522(3)	C(2C)-H(2C)	0.777(17)
C(11A)-H(11A)	0.959(16)	C(3C)-C(4C)	1.461(3)
C(11A)-H(11B)	0.947(18)	C(4C)-C(5C)	1.313(3)
C(12A)-H(12A)	0.989(16)	C(4C)-H(4C)	0.864(17)
C(12A)-H(12B)	0.877(18)	C(5C)-C(6C)	1.516(3)
C(12A)-H(12C)	0.94(2)	C(5C)-H(5C)	0.901(17)
Br(2)-C(1B)	1.8929(18)	C(6C)-C(11C)	1.557(3)
S(1B)-O(2B)	1.4923(12)	C(7C)-C(10C)	1.519(3)
S(1B)-N(1B)	1.6709(16)	C(7C)-C(8C)	1.516(3)
S(1B)-C(7B)	1.8405(19)	C(7C)-C(9C)	1.523(3)
O(1B)-C(3B)	1.230(2)	C(8C)-H(8C1)	0.884(18)
N(1B)-C(6B)	1.487(2)	C(8C)-H(8C2)	0.970(17)
N(1B)-H(1B)	0.802(17)	C(8C)-H(8C3)	1.001(17)
C(1B)-C(2B)	1.326(3)	C(9C)-H(9C1)	1.026(17)
C(1B)-C(6B)	1.510(2)	C(9C)-H(9C2)	0.915(19)
C(2B)-C(3B)	1.468(3)	C(9C)-H(9C3)	0.945(18)
C(2B)-H(2B)	0.850(17)	C(10C)-H(10G)	0.944(18)
C(3B)-C(4B)	1.459(3)	C(10C)-H(10H)	0.983(18)
C(4B)-C(5B)	1.321(3)	C(10C)-H(10I)	0.952(18)
C(4B)-H(4B)	0.956(17)	C(11C)-C(12C)	1.528(3)
C(5B)-C(6B)	1.498(2)	C(11C)-H(11E)	1.01(2)
C(5B)-H(5B)	0.870(18)	C(11C)-H(11F)	1.023(17)

C(12C)-H(12G)	1.008(18)	H(10B)-C(10A)-H(10C)	101.7(16)
C(12C)-H(12H)	1.10(2)	C(12A)-C(11A)-C(6A)	113.45(18)
C(12C)-H(12I)	0.93(2)	C(12A)-C(11A)-H(11A)	107.7(10)
		C(6A)-C(11A)-H(11A)	111.0(10)
O(2A)-S(1A)-N(1A)	112.07(8)	C(12A)-C(11A)-H(11B)	109.9(11)
O(2A)-S(1A)-C(7A)	104.84(8)	C(6A)-C(11A)-H(11B)	107.2(11)
N(1A)-S(1A)-C(7A)	99.80(8)	H(11A)-C(11A)-H(11B)	107.5(15)
C(6A)-N(1A)-S(1A)	115.40(13)	C(11A)-C(12A)-H(12A)	111.2(10)
C(6A)-N(1A)-H(1A)	112.6(15)	C(11A)-C(12A)-H(12B)	110.5(12)
S(1A)-N(1A)-H(1A)	117.1(15)	H(12A)-C(12A)-H(12B)	99.9(15)
C(2A)-C(1A)-C(6A)	124.94(17)	C(11A)-C(12A)-H(12C)	115.8(13)
C(2A)-C(1A)-Br(1)	119.77(15)	H(12A)-C(12A)-H(12C)	110.5(16)
C(6A)-C(1A)-Br(1)	115.23(13)	H(12B)-C(12A)-H(12C)	107.8(17)
C(1A)-C(2A)-C(3A)	121.87(19)	O(2B)-S(1B)-N(1B)	110.72(8)
C(1A)-C(2A)-H(2A)	123.4(12)	O(2B)-S(1B)-C(7B)	104.83(8)
C(3A)-C(2A)-H(2A)	114.7(11)	N(1B)-S(1B)-C(7B)	99.28(8)
O(1A)-C(3A)-C(2A)	122.06(19)	C(6B)-N(1B)-S(1B)	114.29(12)
O(1A)-C(3A)-C(4A)	122.21(18)	C(6B)-N(1B)-H(1B)	111.7(13)
C(2A)-C(3A)-C(4A)	115.73(17)	S(1B)-N(1B)-H(1B)	114.8(12)
C(5A)-C(4A)-C(3A)	121.95(19)	C(2B)-C(1B)-C(6B)	123.94(18)
C(5A)-C(4A)-H(4A)	122.4(12)	C(2B)-C(1B)-Br(2)	119.82(15)
C(3A)-C(4A)-H(4A)	115.6(12)	C(6B)-C(1B)-Br(2)	116.06(13)
C(4A)-C(5A)-C(6A)	124.99(18)	C(1B)-C(2B)-C(3B)	121.9(2)
C(4A)-C(5A)-H(5A)	122.8(11)	C(1B)-C(2B)-H(2B)	120.1(13)
C(6A)-C(5A)-H(5A)	112.2(11)	C(3B)-C(2B)-H(2B)	117.8(12)
N(1A)-C(6A)-C(5A)	110.39(15)	O(1B)-C(3B)-C(4B)	122.4(2)
N(1A)-C(6A)-C(1A)	109.04(15)	O(1B)-C(3B)-C(2B)	121.1(2)
C(5A)-C(6A)-C(1A)	110.46(15)	C(4B)-C(3B)-C(2B)	116.51(18)
N(1A)-C(6A)-C(11A)	107.28(15)	C(5B)-C(4B)-C(3B)	120.8(2)
C(5A)-C(6A)-C(11A)	108.89(15)	C(5B)-C(4B)-H(4B)	120.3(12)
C(1A)-C(6A)-C(11A)	110.74(16)	C(3B)-C(4B)-H(4B)	118.8(12)
C(8A)-C(7A)-C(10A)	112.94(18)	C(4B)-C(5B)-C(6B)	125.9(2)
C(8A)-C(7A)-C(9A)	110.65(17)	C(4B)-C(5B)-H(5B)	122.5(13)
C(10A)-C(7A)-C(9A)	111.22(18)	C(6B)-C(5B)-H(5B)	111.0(13)
C(8A)-C(7A)-S(1A)	109.64(12)	N(1B)-C(6B)-C(5B)	110.73(14)
C(10A)-C(7A)-S(1A)	107.97(13)	N(1B)-C(6B)-C(1B)	109.52(14)
C(9A)-C(7A)-S(1A)	104.01(13)	C(5B)-C(6B)-C(1B)	110.50(16)
C(7A)-C(8A)-H(8A1)	110.2(13)	N(1B)-C(6B)-C(11B)	106.15(15)
C(7A)-C(8A)-H(8A2)	111.9(10)	C(5B)-C(6B)-C(11B)	109.37(15)
H(8A1)-C(8A)-H(8A2)	106.4(16)	C(1B)-C(6B)-C(11B)	110.47(15)
C(7A)-C(8A)-H(8A3)	111.8(11)	C(10B)-C(7B)-C(8B)	112.85(18)
H(8A1)-C(8A)-H(8A3)	107.7(16)	C(10B)-C(7B)-C(9B)	111.09(19)
H(8A2)-C(8A)-H(8A3)	108.6(14)	C(8B)-C(7B)-C(9B)	111.26(18)
C(7A)-C(9A)-H(9A1)	108.1(13)	C(10B)-C(7B)-S(1B)	108.01(14)
C(7A)-C(9A)-H(9A2)	115.5(13)	C(8B)-C(7B)-S(1B)	110.51(14)
H(9A1)-C(9A)-H(9A2)	109.5(18)	C(9B)-C(7B)-S(1B)	102.61(14)
C(7A)-C(9A)-H(9A3)	112.2(12)	C(7B)-C(8B)-H(8B1)	110.1(12)
H(9A1)-C(9A)-H(9A3)	111.3(17)	C(7B)-C(8B)-H(8B2)	111.6(12)
H(9A2)-C(9A)-H(9A3)	100.1(16)	H(8B1)-C(8B)-H(8B2)	102.4(16)
C(7A)-C(10A)-H(10A)	112.4(11)	C(7B)-C(8B)-H(8B3)	112.6(11)
C(7A)-C(10A)-H(10B)	109.0(11)	H(8B1)-C(8B)-H(8B3)	108.1(16)
H(10A)-C(10A)-H(10B)	111.3(15)	H(8B2)-C(8B)-H(8B3)	111.5(16)
C(7A)-C(10A)-H(10C)	110.9(12)	C(7B)-C(9B)-H(9B1)	110.0(12)
H(10A)-C(10A)-H(10C)	111.0(17)	C(7B)-C(9B)-H(9B2)	119.6(15)

H(9B1)-C(9B)-H(9B2)	110.7(19)	N(1C)-C(6C)-C(5C)	110.89(14)
C(7B)-C(9B)-H(9B3)	115.6(13)	N(1C)-C(6C)-C(1C)	108.60(15)
H(9B1)-C(9B)-H(9B3)	98.6(16)	C(5C)-C(6C)-C(1C)	110.28(15)
H(9B2)-C(9B)-H(9B3)	100.2(18)	N(1C)-C(6C)-C(11C)	107.28(14)
C(7B)-C(10B)-H(10D)	112.5(12)	C(5C)-C(6C)-C(11C)	107.68(16)
C(7B)-C(10B)-H(10E)	111.4(13)	C(1C)-C(6C)-C(11C)	112.08(16)
H(10D)-C(10B)-H(10E)	108.8(17)	C(10C)-C(7C)-C(8C)	112.51(18)
C(7B)-C(10B)-H(10F)	108.6(12)	C(10C)-C(7C)-C(9C)	111.21(17)
H(10D)-C(10B)-H(10F)	111.5(18)	C(8C)-C(7C)-C(9C)	110.61(17)
H(10E)-C(10B)-H(10F)	103.7(17)	C(10C)-C(7C)-S(1C)	106.92(14)
C(12B)-C(11B)-C(6B)	114.06(18)	C(8C)-C(7C)-S(1C)	111.00(13)
C(12B)-C(11B)-H(11C)	106.1(13)	C(9C)-C(7C)-S(1C)	104.22(14)
C(6B)-C(11B)-H(11C)	109.5(12)	C(7C)-C(8C)-H(8C1)	107.8(12)
C(12B)-C(11B)-H(11D)	110.7(9)	C(7C)-C(8C)-H(8C2)	112.5(10)
C(6B)-C(11B)-H(11D)	106.9(9)	H(8C1)-C(8C)-H(8C2)	103.0(14)
H(11C)-C(11B)-H(11D)	109.5(15)	C(7C)-C(8C)-H(8C3)	112.1(10)
C(11B)-C(12B)-H(12D)	114.0(12)	H(8C1)-C(8C)-H(8C3)	108.1(15)
C(11B)-C(12B)-H(12E)	112.1(12)	H(8C2)-C(8C)-H(8C3)	112.7(15)
H(12D)-C(12B)-H(12E)	101.4(15)	C(7C)-C(9C)-H(9C1)	112.6(9)
C(11B)-C(12B)-H(12F)	118.9(12)	C(7C)-C(9C)-H(9C2)	112.0(12)
H(12D)-C(12B)-H(12F)	102.0(16)	H(9C1)-C(9C)-H(9C2)	112.0(14)
H(12E)-C(12B)-H(12F)	106.5(15)	C(7C)-C(9C)-H(9C3)	106.0(12)
O(2C)-S(1C)-N(1C)	110.32(8)	H(9C1)-C(9C)-H(9C3)	112.0(15)
O(2C)-S(1C)-C(7C)	104.89(8)	H(9C2)-C(9C)-H(9C3)	101.6(16)
N(1C)-S(1C)-C(7C)	100.00(8)	C(7C)-C(10C)-H(10G)	109.8(12)
C(6C)-N(1C)-S(1C)	117.11(12)	C(7C)-C(10C)-H(10H)	108.1(13)
C(6C)-N(1C)-H(1C)	116.4(11)	H(10G)-C(10C)-H(10H)	108.3(16)
S(1C)-N(1C)-H(1C)	114.4(12)	C(7C)-C(10C)-H(10I)	108.6(11)
C(2C)-C(1C)-C(6C)	125.51(18)	H(10G)-C(10C)-H(10I)	113.9(16)
C(2C)-C(1C)-Br(3)	119.91(16)	H(10H)-C(10C)-H(10I)	107.9(16)
C(6C)-C(1C)-Br(3)	114.58(13)	C(12C)-C(11C)-C(6C)	112.65(17)
C(1C)-C(2C)-C(3C)	121.5(2)	C(12C)-C(11C)-H(11E)	111.8(11)
C(1C)-C(2C)-H(2C)	120.4(15)	C(6C)-C(11C)-H(11E)	105.5(12)
C(3C)-C(2C)-H(2C)	118.1(15)	C(12C)-C(11C)-H(11F)	109.6(10)
O(1C)-C(3C)-C(2C)	121.6(2)	C(6C)-C(11C)-H(11F)	111.4(10)
O(1C)-C(3C)-C(4C)	122.4(2)	H(11E)-C(11C)-H(11F)	105.6(14)
C(2C)-C(3C)-C(4C)	115.94(18)	C(11C)-C(12C)-H(12G)	109.7(10)
C(5C)-C(4C)-C(3C)	122.3(2)	C(11C)-C(12C)-H(12H)	111.2(12)
C(5C)-C(4C)-H(4C)	121.7(13)	H(12G)-C(12C)-H(12H)	111.9(16)
C(3C)-C(4C)-H(4C)	115.8(13)	C(11C)-C(12C)-H(12I)	108.2(14)
C(4C)-C(5C)-C(6C)	124.19(19)	H(12G)-C(12C)-H(12I)	117.4(17)
C(4C)-C(5C)-H(5C)	122.4(12)	H(12H)-C(12C)-H(12I)	98.0(18)
C(6C)-C(5C)-H(5C)	113.3(12)		

Table A2.4. Anisotropic displacement parameters ($Å^2 x\ 10^4$) for RUN02 (CCDC 780836). The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	290(1)	195(1)	416(1)	73(1)	92(1)	-18(1)
S(1A)	142(2)	172(2)	140(3)	1(2)	13(2)	9(2)
O(1A)	290(8)	349(9)	232(9)	-12(7)	76(7)	118(7)
O(2A)	210(7)	205(7)	188(7)	65(6)	55(6)	-21(6)
N(1A)	186(8)	144(9)	143(9)	-24(8)	22(7)	34(7)
C(1A)	167(9)	159(10)	208(11)	32(9)	-33(8)	11(8)
C(2A)	233(10)	153(11)	224(12)	-12(9)	0(9)	40(9)
C(3A)	195(10)	257(11)	153(11)	43(9)	-43(8)	73(8)
C(4A)	145(9)	250(12)	246(12)	42(10)	24(8)	-19(8)
C(5A)	140(8)	151(10)	219(11)	1(9)	-39(8)	16(8)
C(6A)	148(9)	148(10)	140(10)	3(8)	10(8)	37(7)
C(7A)	130(9)	161(10)	203(11)	10(9)	-4(8)	13(7)
C(8A)	181(10)	215(12)	243(13)	-14(10)	13(9)	22(9)
C(9A)	219(11)	383(15)	285(14)	-82(12)	-78(10)	68(11)
C(10A)	144(10)	232(13)	464(17)	8(12)	13(11)	-14(9)
C(11A)	226(10)	246(12)	195(12)	-19(10)	11(9)	78(9)
C(12A)	300(12)	328(15)	165(13)	-10(11)	-51(10)	109(10)
Br(2)	218(1)	328(1)	391(1)	-72(1)	103(1)	-69(1)
S(1B)	214(2)	155(2)	113(2)	11(2)	14(2)	-32(2)
O(1B)	891(14)	204(9)	562(13)	138(9)	-162(11)	11(9)
O(2B)	255(7)	246(8)	155(7)	16(6)	-34(6)	4(6)
N(1B)	188(8)	154(9)	136(9)	18(7)	44(7)	-40(7)
C(1B)	262(10)	205(11)	113(10)	-56(9)	32(8)	-59(8)
C(2B)	429(13)	203(12)	161(11)	-10(9)	22(10)	-151(10)
C(3B)	606(16)	168(12)	238(13)	-30(10)	-127(11)	8(11)
C(4B)	332(12)	240(13)	381(15)	-76(11)	-51(11)	61(10)
C(5B)	238(11)	227(12)	258(13)	-50(10)	27(9)	-3(9)
C(6B)	209(8)	128(9)	139(10)	-23(9)	16(7)	-39(8)
C(7B)	266(10)	142(10)	160(11)	-20(9)	49(8)	-43(8)
C(8B)	329(12)	156(11)	308(15)	-10(11)	112(11)	-67(10)
C(9B)	643(18)	193(13)	217(14)	-72(11)	106(13)	5(13)
C(10B)	287(11)	241(13)	348(15)	23(11)	100(11)	23(10)
C(11B)	264(10)	222(11)	159(11)	5(10)	52(9)	-70(9)
C(12B)	394(13)	294(14)	168(13)	-100(11)	40(11)	-97(11)
Br(3)	447(1)	242(1)	407(1)	120(1)	172(1)	27(1)
S(1C)	177(2)	196(3)	126(3)	-15(2)	14(2)	-28(2)
O(1C)	475(10)	492(11)	495(12)	-84(9)	-280(9)	137(9)
O(2C)	249(7)	195(7)	225(8)	60(6)	19(6)	-42(6)
N(1C)	177(8)	202(9)	133(9)	-32(7)	15(7)	6(7)
C(1C)	212(9)	196(10)	196(11)	40(9)	75(8)	45(9)
C(2C)	194(9)	192(11)	356(13)	-75(11)	35(9)	-26(10)
C(3C)	223(10)	322(13)	257(13)	-59(11)	-59(9)	109(9)
C(4C)	287(11)	239(12)	225(12)	82(10)	41(10)	116(9)
C(5C)	251(11)	163(11)	278(13)	-4(10)	72(9)	8(9)

C(6C)	161(9)	208(10)	135(10)	1(9)	21(8)	23(8)
C(7C)	235(10)	162(10)	189(11)	-26(8)	55(8)	1(8)
C(8C)	257(10)	263(13)	248(13)	-48(11)	6(9)	77(10)
C(9C)	260(12)	326(14)	254(13)	-74(11)	88(10)	-11(10)
C(10C)	400(13)	183(12)	442(16)	-32(13)	156(12)	16(11)
C(11C)	278(11)	307(13)	199(12)	-55(11)	26(9)	22(10)
C(12C)	343(13)	357(15)	277(14)	-61(12)	79(11)	108(11)

Table A2.5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for RUN02 (CCDC 780836).

	x	y	z	U_{iso}
H(1A)	680(17)	9690(10)	10696(14)	1(5)
H(2A)	2878(17)	7459(10)	9401(14)	23(6)
H(4A)	4585(19)	9508(11)	9152(14)	32(6)
H(5A)	3230(16)	10006(9)	10348(13)	13(5)
H(8A1)	-1307(19)	10787(11)	9363(15)	32(6)
H(8A2)	-1397(18)	10393(10)	10416(15)	24(5)
H(8A3)	-2715(18)	10554(10)	9553(14)	25(5)
H(9A1)	-3050(20)	9806(11)	7845(16)	43(7)
H(9A2)	-1970(20)	9295(12)	7475(16)	49(7)
H(9A3)	-1707(19)	10087(10)	7534(15)	27(6)
H(10A)	-1772(18)	8989(10)	10362(15)	23(6)
H(10B)	-1812(19)	8532(11)	9239(16)	35(6)
H(10C)	-2966(19)	8987(10)	9466(14)	22(5)
H(11A)	1808(16)	8876(9)	12208(13)	9(5)
H(11B)	2591(18)	9603(11)	12058(14)	27(6)
H(12A)	3719(16)	8132(9)	12208(13)	16(5)
H(12B)	3999(17)	8716(10)	12986(15)	19(6)
H(12C)	4600(20)	8842(11)	12008(16)	37(7)
H(1B)	2260(17)	441(10)	7606(13)	14(5)
H(2B)	4155(17)	2724(10)	6114(13)	18(5)
H(4B)	224(17)	2638(11)	6600(14)	28(5)
H(5B)	844(18)	1619(11)	7647(14)	26(6)
H(8B1)	1589(18)	-1388(11)	6532(15)	22(5)
H(8B2)	751(18)	-732(10)	6410(15)	21(6)
H(8B3)	1897(19)	-781(11)	7420(16)	35(6)
H(9B1)	2860(20)	-511(11)	4366(15)	35(6)
H(9B2)	1340(20)	-670(13)	4447(19)	63(9)
H(9B3)	2350(18)	-1206(11)	4625(15)	24(6)
H(10D)	4325(19)	-557(11)	7037(16)	31(6)
H(10E)	4640(20)	-503(12)	5916(17)	46(7)
H(10F)	4188(18)	-1241(12)	6290(16)	33(6)
H(11C)	2666(18)	1320(11)	9099(14)	28(6)
H(11D)	4213(17)	1188(10)	8913(14)	28(5)
H(12D)	4276(19)	2590(12)	8910(14)	44(6)
H(12E)	3795(16)	2316(10)	9895(14)	17(5)
H(12F)	2760(20)	2679(13)	9065(15)	47(7)
H(1C)	-61(17)	5901(10)	5955(14)	19(5)
H(2C)	4390(19)	6797(10)	7546(16)	33(7)
H(4C)	3426(18)	4836(10)	8550(14)	19(6)
H(5C)	1695(18)	4768(10)	7196(14)	24(6)
H(8C1)	-3048(18)	6886(10)	6336(14)	26(6)
H(8C2)	-2699(17)	6101(10)	6516(14)	17(5)
H(8C3)	-1971(17)	6612(10)	5679(14)	23(5)
H(9C1)	-1266(16)	7081(10)	8972(13)	18(5)
H(9C2)	-2431(18)	6514(11)	8445(14)	30(6)
H(9C3)	-2649(19)	7294(11)	8168(15)	35(6)

H(10G)	-172(18)	7526(11)	6447(15)	29(6)
H(10H)	43(19)	7728(12)	7665(15)	41(7)
H(10I)	-1299(18)	7979(10)	6953(14)	21(5)
H(11E)	1320(20)	4978(11)	5276(16)	41(7)
H(11F)	1625(17)	5765(10)	4720(14)	16(5)
H(12G)	4043(18)	5574(10)	5207(14)	25(6)
H(12H)	3370(20)	4825(13)	4412(19)	71(8)
H(12I)	3640(20)	4733(12)	5633(19)	55(8)

Table A2.6. Hydrogen bonds for RUN02 (CCDC 780836) [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1A)-H(1A)...O(2C)#1	0.692(16)	2.219(16)	2.897(2)	167(2)
N(1B)-H(1B)...O(2A)#2	0.802(17)	2.148(17)	2.9066(19)	158.0(17)
N(1C)-H(1C)...O(2B)#3	0.876(17)	2.001(17)	2.834(2)	158.6(16)

Symmetry transformations used to generate equivalent atoms:
#1 -x,y+1/2,-z+2
#2 x,y-1,z
#3 -x,y+1/2,-z+1

CHAPTER 3

An Introduction to Acutumine

3.1. Introduction

A second collection of alkaloids that exhibit the azapropellane structural framework is exemplified by acutumine (**133**, Figure 1). In contrast to its hasubanan counterparts, acutumine bears a [4.3.3] propellane backbone adorned with a spirocyclic cyclopentenone moiety. Embedded within this densely functionalized molecule are five contiguous stereocenters, two of which are all-carbon quaternary centers. Additionally, one of the stereogenic carbons bears a neopentylic chloride. Since the original structural elucidation of **133** in the late 1960s, a total of 12 related alkaloids have been identified to date, which possess slight variations in their oxidation state and peripheral structure (see Figure 1).

In addition to its unique structural architecture, acutumine has been found to exhibit distinctive medicinal properties, including selective T-cell cytotoxicity[1] and antiamnesic properties.[2] More recently, dauricumidine (**136**) was found to display modest cytoxicity

against a hepatitis B virus-transfected cell line.[3] Not surprisingly, these structural and biological properties have attracted considerable attention from the synthetic community. This chapter is intended to present a brief introduction to acutumine, beginning with its isolation, characterization, and potential biosynthetic origins. This background will lead into a discussion of the synthetic approaches toward this challenging target.

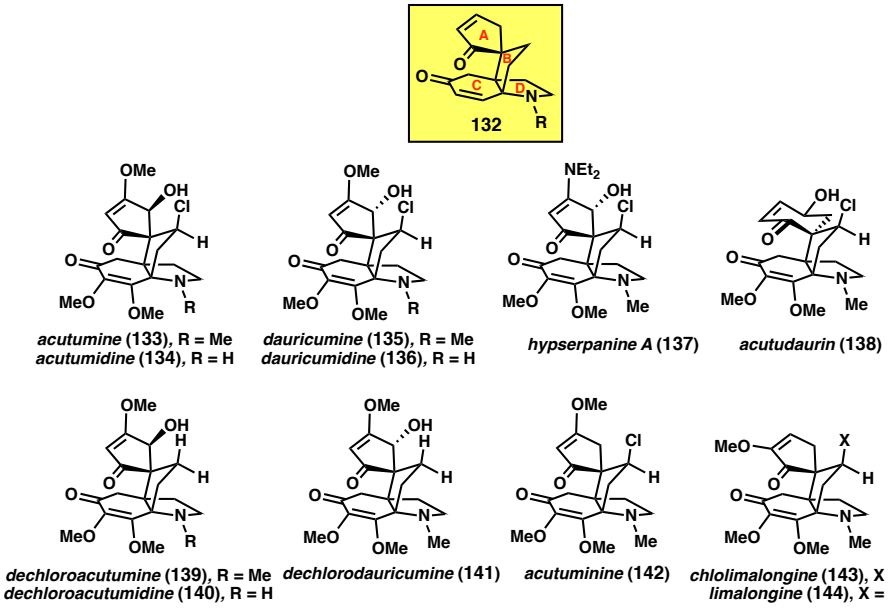


Figure 1. The acutumine alkaloids.

3.2. Isolation

In 1929, Goto and Sudzuki reported the isolation of acutumine from *Sinomenium acutum*, a climbing plant of the Menispermaceae family.[4] However, its molecular formula was misassigned as $C_{20}H_{27}NO_8$. Tomita and coworkers corrected it to $C_{19}H_{24}NO_6Cl$ in 1967, when they conducted an extensive spectroscopic and chemical analysis of the natural product.[5] In this series of studies, the authors also obtained an X-ray crystal structure of **133**, thereby confirming their structural assignment. The absolute

configuration of acutumine was determined via comparison of its CD spectral patterns with those of hasubanonine.[6] Using this data, the authors also elucidated the structure of acutumidine (**134**), a natural product they isolated alongside **133**.

Over two decades elapsed before other natural products bearing the acutumine framework began to emerge. The new alkaloids were characterized by comparison of their spectral data to that of acutumine.[1,3,7-10] These acutumine analogs mainly differ in (1) the presence of a stereogenic C-Cl bond, and (2) the composition of the spirocyclic enone. These structural differences can be subtle—such as the epimeric relationship between **133** and dauricumine—or more pronounced, as is the case with the cylcohexenone-bearing acutudaurin (**138**). These slight deviations from the common spirocycle-containing [4.4.3] propellane framework have led to queries regarding the biosynthetic origins of the acutumine alkaloids. These studies are discussed in detail below.

3.3. Biosynthesis

As part of their studies regarding the biosynthesis of several morphinan alkaloids, Barton and coworkers put forth a biosynthetic pathway for acutumine.[11] The authors speculated that isoquinoline derivative **145** undergoes intramolecular phenol coupling to deliver spirocycle **146**. Sequential epoxidation of this intermediate provides diepoxide **147**, an intermediate proposed to undergo a Favorskii-type rearrangement to install the A ring of the natural product. Acid **148** can be elaborated to cyclopentenone **150** via a decarboxylative epoxide opening followed by oxidation of the resulting diol. To establish the propellane core, the quinone functionality of **150** is hypothesized to undergo

nucleophilic attack by the pendant isoquinoline nitrogen, thereby furnishing aziridinium ion **151**. A 1,2-hydride shift can then afford carbocation **152**, which upon nucleophilic attack by a chloride anion and D-ring isomerization can yield the natural product.

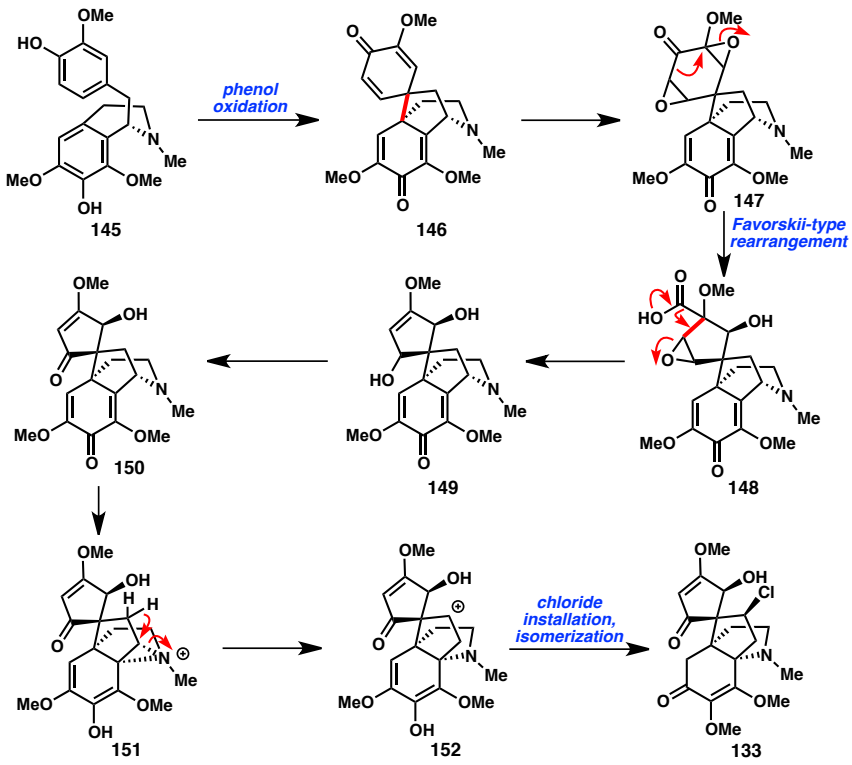


Figure 2. Barton's proposed biosynthesis of the spirocyclic cyclopentenone.

While Barton's proposal offers intriguing biosynthetic transformations, the authors present limited experimental data to verify this potential route. To examine the feasibility of a Favorskii-type cyclopentenone formation, Matoba and coworkers set out to prepare and examine the reactivity of a simple model substrate, epoxide **153**.[12] Exposure of epoxyenone **153** to *m*-CPBA in refluxing 1,1,1-trichloroethane delivered lactone **154** in 52% yield. Unfortunately, other attempts to prepare bisepoxide **155** from the corresponding dienone proved unfruitful. More recently, Wipf and coworkers were met

with a similar reactivity patterns. In their case, addition of **153** to a buffered solution of *m*-CPBA in CH_2Cl_2 only provided epoxylactone **159**.[13] The formation of **159** is speculated to arise from an initial epoxide opening of **156**, which generates the corresponding oxocarbenium ion. Peracid addition to this oxocarbenium ion delivers **157**, an intermediate hypothesized to undergo a Baeyer-Villiger ring expansion and translactonization reaction to form **159**.

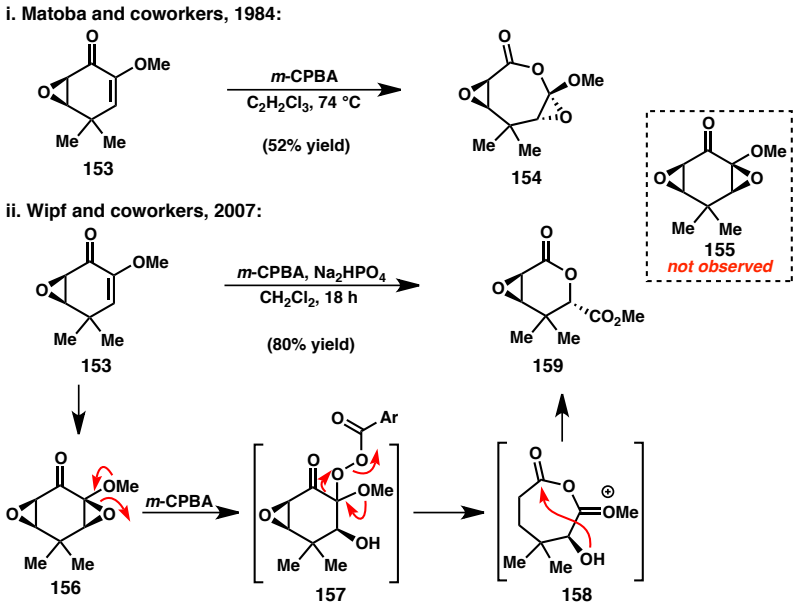


Figure 3. Bisepoxidation studies by Matoba and Wipf.

Based on this unexpected reactivity, Wipf and coworkers put forth an alternative mechanism for cyclopentenone biosynthesis. In this scenario, epoxidation of dienol **160** initially yields ketone hydrate **162**, which is converted to **163** via a semipinacol-type rearrangement. Decarboxylation of **163** is then thought to establish the cyclopentenone moiety of acutumine. Interestingly, the authors posit that the isolation of acutudaurin

(**138**, see Figure 1), a potential acutumine alkaloid precursor, provides further evidence for their biosynthetic proposal.

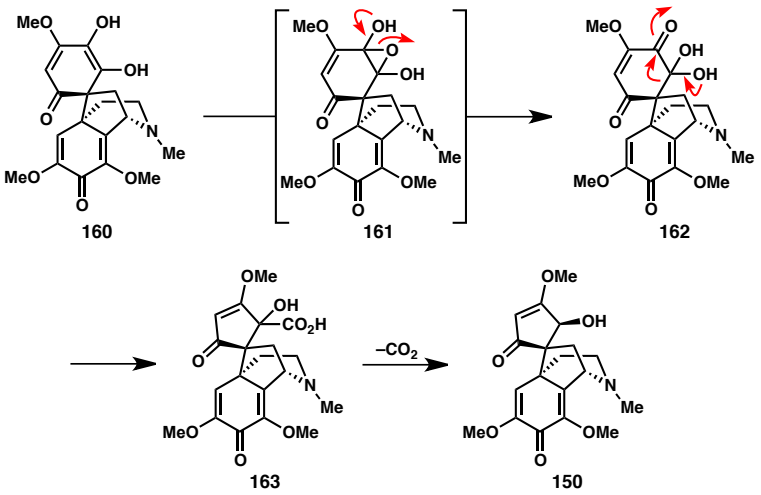


Figure 4. Wipf's biosynthetic proposal.

While the studies discussed above present plausible reaction pathways for acutumine biosynthesis, thorough biological investigations to probe these mechanistic possibilities are limited. In 1999, Sugimoto and coworkers conducted feeding experiments with ^{13}C-labeled tyrosine, which demonstrated that two molecules of tyrosine are incorporated into acutumine.[14] Additionally, the authors found that ^{3}H-labeled dechloroacutumine (**134**, see Figure 5) can be converted to **133** in vitro, suggesting that dechloroacutumine is a precursor of **133**. To further investigate the potential interrelationship between the acutumine alkaloids, Sugimoto more recently disclosed feeding experiments using ^{36}Cl-labeled **133**-**136** in *Menispermum dauricum* root cultures (Figure 5).[9] These studies revealed a mutual interconversion between each pair of *N*-alkyl and *N*-H compounds (e.g., **133** and **134**, **135** and **136**). Moreover, the authors determined that dauricumine

could be epimerized to acutumine; however, the converse relationship was not observed. This collective data suggests that dauricumine (**135**) is a biogenetic precursor to **133**, **134**, and **136**.

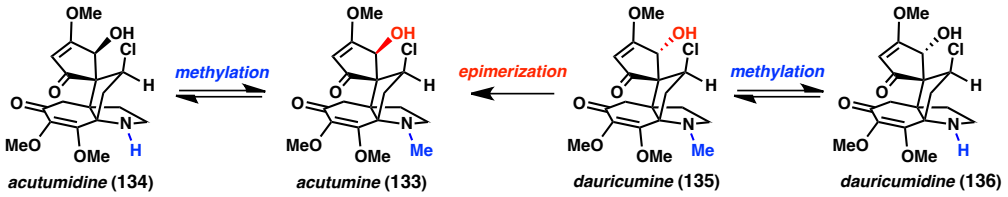


Figure 5. Potential interconversion between the acutumine alkaloids.

In spite of these biosynthetic investigations, there remain a number of aspects of the proposed pathway that need to be addressed. Although a number of parallels can be drawn between propellane formation of acutumine and the hasubanan alkaloids,[15] mechanistic studies that probe this key transformation in the context of acutumine have not been reported. Moreover, chloride installation remains an elusive mechanistic query. Barton suggests nucleophilic attack by a chloride anion to be an operative mechanism; on the other hand, a wealth of literature data suggests that organochlorides are commonly bioengineered via electrophilic chlorination reactions.[16] Further studies that carefully examine these potential biogenetic pathways will ultimately deepen our understanding of propellane alkaloid synthesis.

3.4. Previous Synthetic Studies

Despite the fact that its structure was elucidated over 40 years ago, acutumine remains a challenging target for total synthesis endeavors. Indeed, only two completed

syntheses of acutumine have been reported to date. The discussion below showcases existing strategies toward the acutumine alkaloids, and focuses on the key transformations of each.

3.4.1. Sorensen's Strategy

In 2007, Sorensen and Moreau reported their synthetic approach toward acutumine. Specifically, the authors sought to harness the reactivity of enolates to construct the propellane framework.[17] To this end, readily available pyrrolidinone **164** was advanced to alkyne **166** following an enolate alkylation/Grignard addition reaction sequence. Exposure of **166** to $VO(acac)_2$ and *t*-BuOOH facilitated a directed epoxidation of the pendant olefin, thereby delivering **167** in good yield. Palladium-catalyzed carbonylative cyclization of **167** afforded the corresponding vinylogous ester, which was subjected to periodate-mediated oxidation to yield ketone **168**.

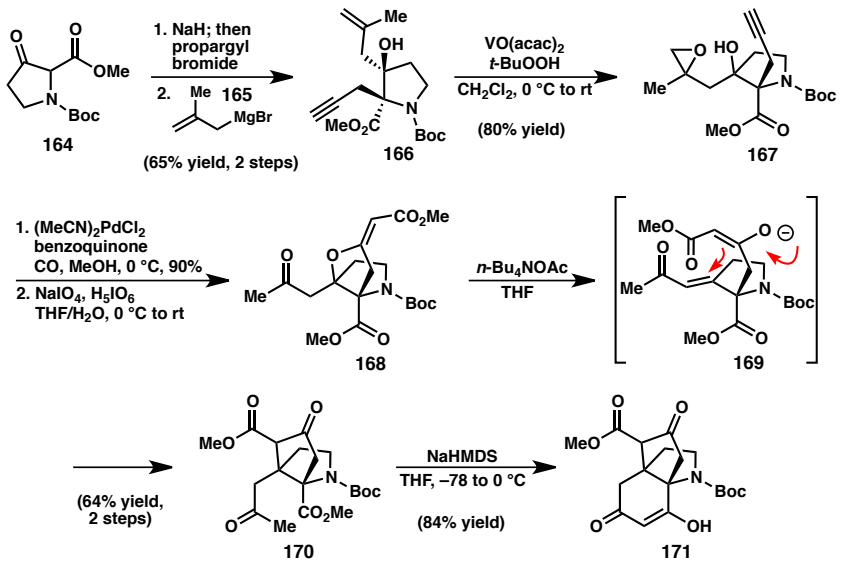


Figure 6. Sorensen's approach to acutumine.

In a key step in their synthesis, the authors found that treatment of **168** with a mild base unveils enolate **169**, which immediately attacks the α,β-unsaturated ketone moiety to afford β-ketoester **170**. The D ring of acutumine was then constructed by a Dieckmann cyclization, which yielded propellane **171** in 84% yield. Using this sequence, **171** could be accessed in 10 steps from commercially available starting materials. Unfortunately, attempts to advance this and similar intermediates to the natural product have proven unfruitful.[18,19]

3.4.2. Castle's Total Synthesis

The first total synthesis of acutumine was accomplished by Castle and coworkers in 2009.[20] Their synthetic efforts commenced with Weinreb amide **173**, an intermediate that suffers nucleophilic attack by the Grignard reagent of vinyl iodide **172** to give enone **174**. Selective 1,2-reduction of the ketone was effected using the Corey-Bakshi-Shibata (CBS) catalyst, and the resulting alcohol was treated with $MsCl/Et_3N$ to furnish chloride **175** in 59% yield over two steps. Enone **176** could be prepared from **175** via cleavage of the TES group and subsequent oxidation of the free alcohol.

With access to **176**, the authors were poised to examine a radical-polar crossover reaction to install the 5,5-spirocycle of the natural product. After a screen of reaction parameters,[21] the desired transformation was effected by irradiation of **176** in the presence of $(Bu_3Sn)_2/Et_3Al$ followed by addition of oxaziridine **177**, ultimately providing **178** in 69% yield. After an additional five steps, **178** could be elaborated to *o*-quinone monoketal **179**. Allylation of this intermediate with chiral allylzinc reagent **180** afforded alcohol **181** in good yield and excellent diastereoselectivity. At this point, the ethylamine

bridge was installed following a three-step sequence involving oxy-Cope rearrangement, ozonolysis of the resulting olefin, and reductive amination. Finally, the pyrrolidine ring of **133** was constructed by treatment of amine **182** with BCl_3, which provided propellane **183** in 45% yield. Additional functional group manipulations led to the synthesis of acutumine (**133**) in a total of 29 steps from commercially available starting materials.

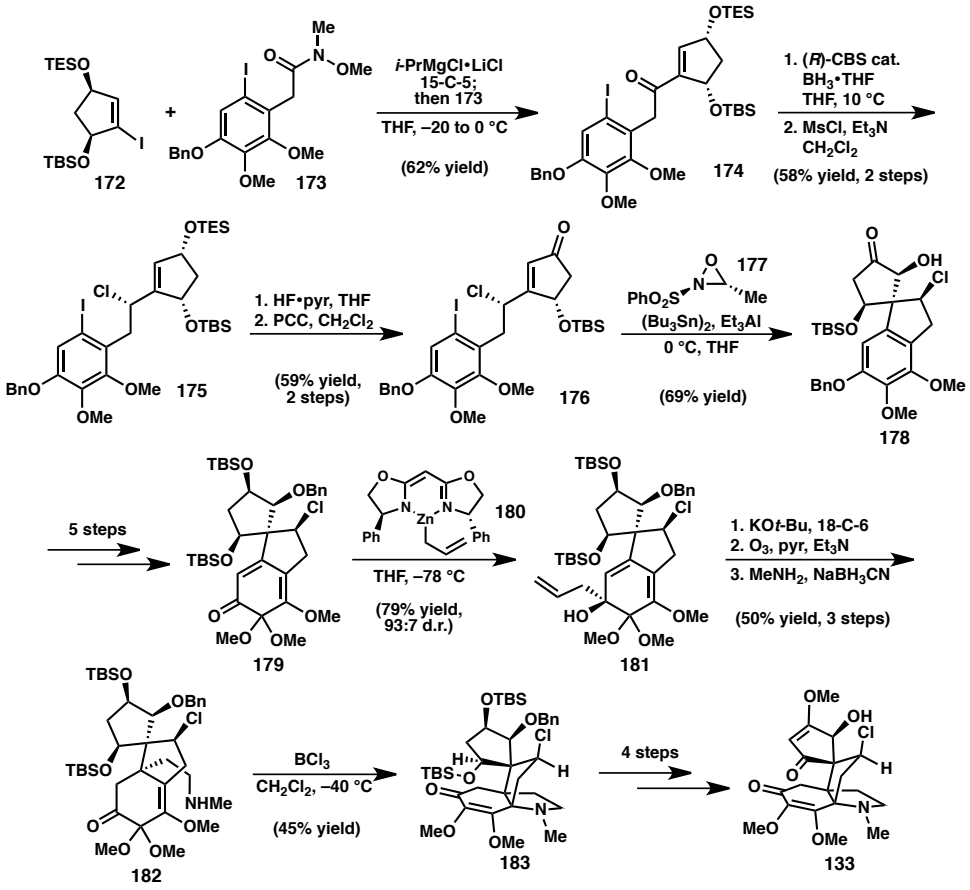


Figure 7. Castle's total synthesis of acutumine.

3.4.3. Herzon's Total Synthesis

The Herzon group recently disclosed their efforts toward a number of propellane alkaloids, which has culminated in the preparation of acutumine.[22] In accord with their

synthetic strategy toward the hasubanan alkaloids,[23] treatment of **184** with MeOTf followed by addition of organolithium **185** at –90 °C afforded 1,2-addition product **186** in 85% yield (Figure 8). Thermal extrusion of 5-trimethylsilylcyclopentadiene and hydrostannylation of **186** delivered dienone **187**. Moving forward, the authors were able to install both all-carbon quaternary stereocenters in a single step by treatment of **187** with TBAF in DMF; however, this key reaction furnishes **188** in only 37% yield.

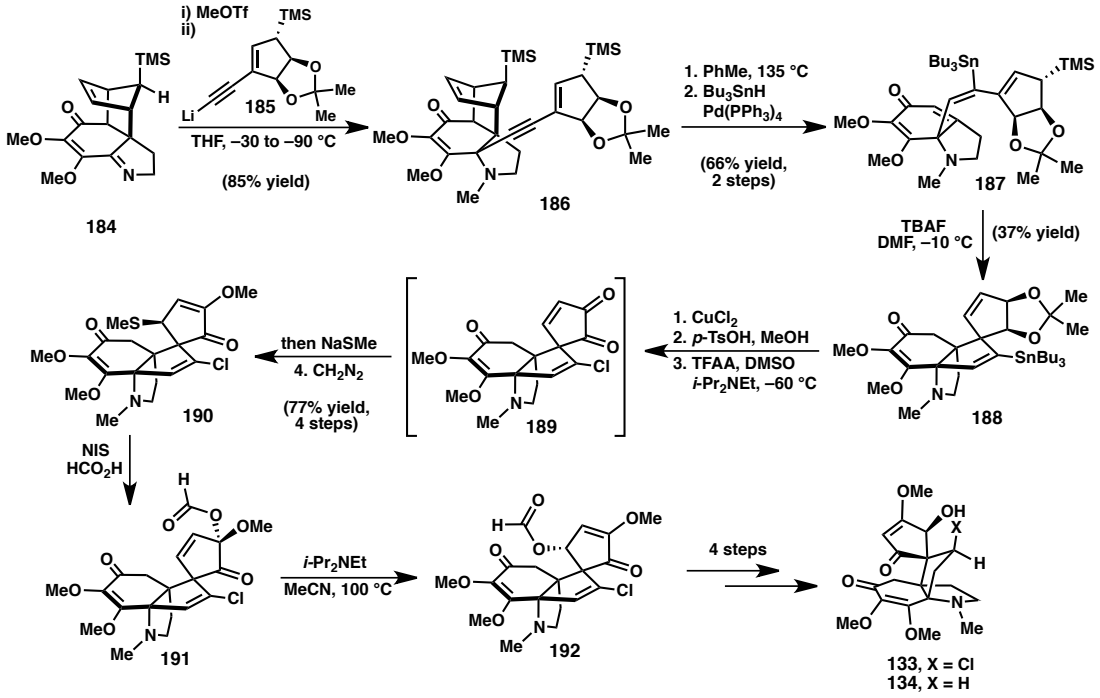


Figure 8. Herzon's synthesis of **133** and **134**.

At this point, completion of the synthesis required installation of the chloride and elaboration of the A-ring (see Figure 1, **132**) to the requisite cyclopentenone. Toward this goal, chlorodestannylation and acid-mediated acetonide cleavage afforded the corresponding diol, which was oxidized to diketone **189**. In situ trapping of **189** with

sodium methanethiolate and treatment with diazomethane yielded methoxyenone **190**. Activation of the sulfide with *N*-iodosuccinimide in formic acid promoted the formation of mixed ketal **191**, an intermediate subjected to thermal [3,3] sigmatropic rearrangement conditions to deliver formate ester **192**. In four additional steps, the authors could advance **192** to acutumine (**133**) and dechloroacutumine (**134**).

3.5. Concluding Remarks

Almost 50 years have elapsed since the first investigations regarding the biosynthesis and structure of acutumine were reported. Despite its decades of history, this alkaloid remains an elusive target for total chemical synthesis. Nevertheless, the studies discussed in this chapter highlight our ability as synthetic chemists to implement novel synthetic technologies toward densely functionalized, polycyclic alkaloid natural products. As new members of this family continue to emerge, it will become increasingly important to develop novel and efficient approaches to access these complex alkaloids.

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CHAPTER 4

Progress Toward the Total Synthesis of Acutumine[†]

4.1. Introduction

Acutumine arguably represents one of the most structurally complex propellane alkaloids. As was discussed in the previous chapter, its promising biological properties and densely functionalized architecture render this molecule an attractive, yet formidable synthetic target. A comparison of the studies discussed in Section 3.4 reveals two significant, commonly encountered challenges in the synthesis of acutumine: the efficient construction of the two vicinal, all-carbon quaternary stereocenters, and stereoselective installation of the chloride. With these considerations in mind, an efficient route to acutumine that utilizes the diastereoselective 1,2-addition to benzoquinone-derived sulfinimines developed in our laboratory was envisioned. Our synthetic plan is discussed in detail below.

[†] Portions of this chapter have been reproduced from published studies (see reference 5) and the supporting information found therein. The research presented in this chapter was completed in collaboration with John R. Butler, a postdoctoral scholar in the Reisman group.

4.2. Synthetic Approach

In a retrosynthetic sense, acutumine (**133**) was simplified to diol **193**, an intermediate envisioned to arise from lactol **195** by a retro-aldol/aldol sequence (Figure 1). In this key reaction, the strained nature of the cyclobutane embedded within pentacycle **195** was expected to facilitate cleavage of the C4-C5 bond to give keto-aldehyde **194**, which could then undergo intramolecular aldol ring closure. While on first inspection, lactol **195** appears to be a complex structural framework, we hypothesized that its cyclobutane core could be constructed in a straightforward fashion by a photochemical [2+2] cycloaddition. This disconnection reduces our target to dihydroindolone **197**, a structural motif readily obtained using the previously developed sulfinimine chemistry.

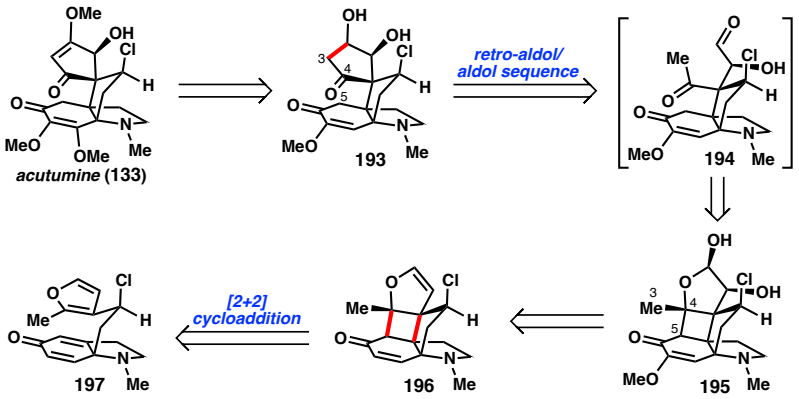


Figure 1. Retrosynthetic analysis of acutumine.

Alternatively, we recognized that isomeric dihydroindolone **202** could also be a viable intermediate en route to acutumine (Figure 2). Indeed, [2+2] cycloaddition and oxidation of this substrate would deliver diol **200**, which can undergo the retro-aldol fragmentation to afford α-hydroxyketone **199**. Intramolecular aldol reaction of **199** would

produce cyclopentanone **198**, a structural isomer of **193** also anticipated to be amenable to the synthesis of acutumine.

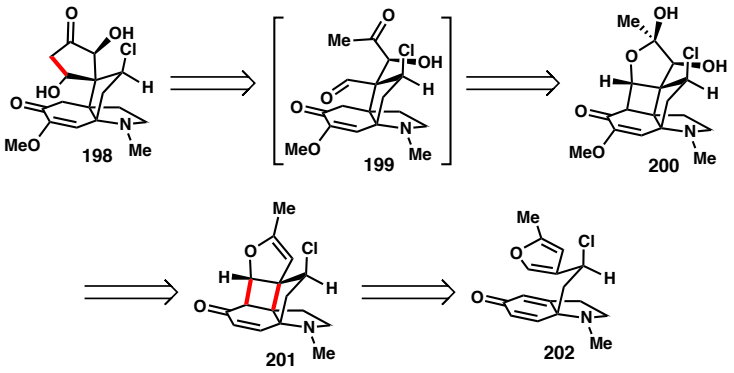


Figure 2. Alternative retro-aldol/aldol precursor.

The synthesis of dihydroindolones **197** and **202** raises questions regarding a key component to our synthetic planning: installation of the stereogenic C–Cl bond. Specifically, the preparation of **197** and **202** using our 1,2-addition methodology necessitates the use of a nucleophile bearing an appropriate functional handle to advance to the chloride. It was envisioned that addition of a furan-derived enolate (**203**) to bromosulfinimine **96c** (Figure 3). Addition of such nucleophiles to *t*-butanesulfinimines is not unprecedented: Ellman and coworkers have demonstrated that 1,2-addition of simple enolates to sulfinyl ketimines generates β-amino acid derivatives in excellent yield and diastereoselectivity.[1] If successful, the resulting ketone-containing sulfinamides could be elaborated to **197** and **202** following our previously optimized cross-coupling/acid cyclization sequence.[2,3]

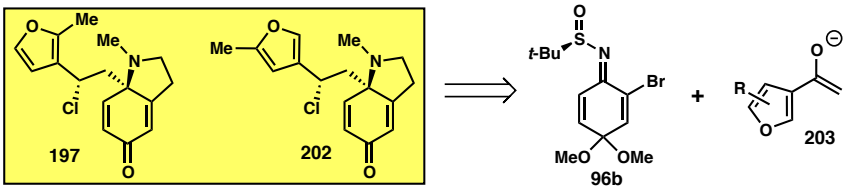


Figure 3. A diastereoselective enolate addition approach for **197** and **202**.

Alternatively, it was anticipated that the [2+2] cycloaddition/retro-aldol/aldol strategy could be assessed by exploring the synthesis of des-chloro dihydroindolones **207** and **208** (Figure 4). Importantly, these substrates were expected to be readily accessible by addition of the appropriate furan-containing Grignard reagent to bromosulfinimine **96c** and elaboration using our previously established conditions. In addition to simplifying substrate preparation, this retrosynthetic modification also presents an opportunity to evaluate a late-stage chlorination via C–H activation chemistry (**204** to **193**). While reports of C–H activation occurring at secondary positions are limited, intermediates such as **204** represent an exciting new platform to develop novel C–H functionalization reactions.

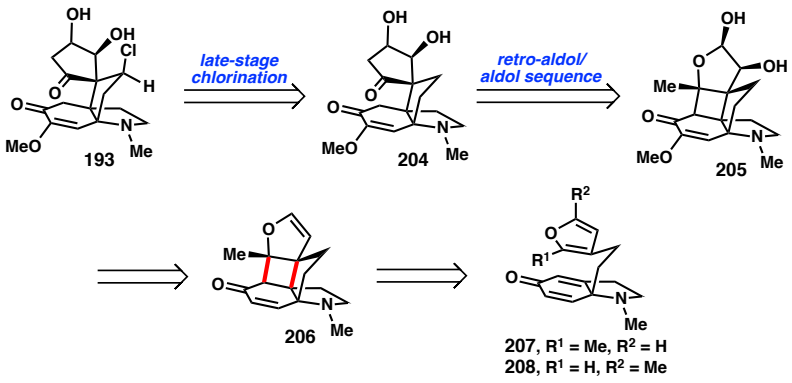


Figure 4. A late-stage chlorination approach.

4.3. Synthetic Investigations

4.3.1. An Enolate 1,2-Addition Strategy. To ascertain the potential utility of an enolate 1,2-addition strategy, initial studies sought to explore the reactivity of ketofuran **209**. We were pleased to find that exposure of **96c** to the sodium enolate of **209** at –78 °C affords sulfinamide **210** in 98% yield and excellent diastereoselectivity (Figure 5). Unfortunately, quenching the sulfinamide anion with MeI and HMPA under our previously optimized conditions[3] delivered an intractable mixture of products. Attempts to alkylate the sulfinamide in a separate step with a variety of methylating reagents revealed that **210** is unstable under basic conditions. On the other hand, cross-coupling of sulfinamide **210** with stannane **105** proceeded without incident; however, subjection of **211** to our optimal cyclization conditions (HCl, THF, 0 °C) led to significant decomposition.

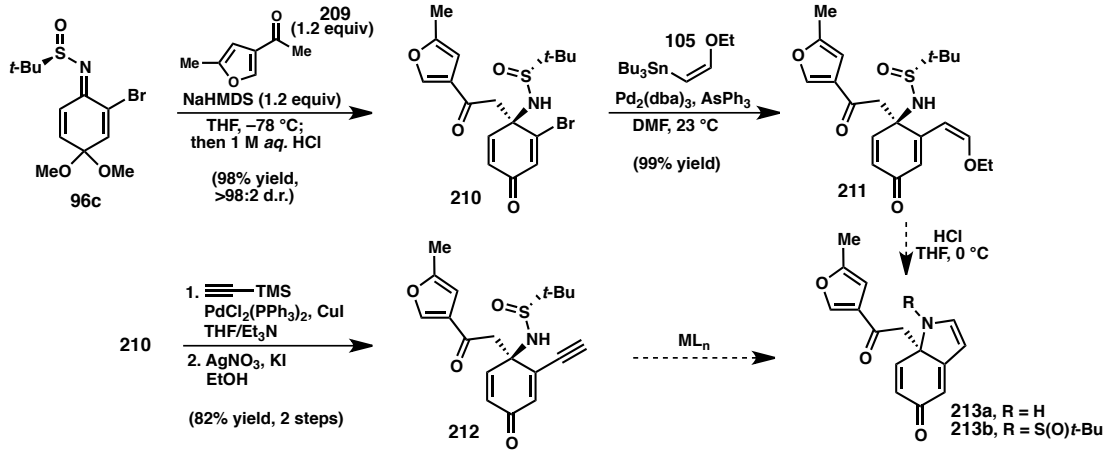


Figure 5. Attempts to prepare indolone **213**.

Moving forward, it was hypothesized that the requisite pyrrolidine ring could potentially be installed via an intramolecular hydroamination of alkyne-bearing

sulfinamide **212** (Figure 4). Importantly, a number of strategies have emerged that accomplish this type of transformation under mild reaction conditions.[4] To evaluate this approach, **212** was prepared in two steps from **210** following Sonogashira coupling with trimethylsilylacetylene and deprotection of the silyl-protected alkyne. To our dismay, attempts to promote the hydroamination with a number of transition metal catalysts only returned starting material or led to decomposition.

4.3.2. An Alkyl Grignard Addition Approach. Based on these initial challenges, we turned our attention to the preparation of des-chloro dihydroindolones **207** and **208** (Figure 6). To this end, we examined the use of furan-containing Grignard reagents **214** and **216** in the sulfinimine methodology. Exposure of bromosulfinimine **96c** to Grignard reagent **214** at –78 °C resulted in the expected 1,2-addition reaction; however, upon purification by flash chromatography, the major product was enol ether **215** (Figure 6).[5] Presumably, the mildly acidic silica gel mediates an intramolecular Friedel–Crafts conjugate addition. Although it might be possible to identify purification conditions that allow for isolation of the 1,2-addition product, the acid sensitivity of this substrate suggests it would not be amenable to pyrrolidine formation using the previously established conditions. We hypothesized that in the analogous 2,3-disubstituted furanyl substrate (**216**), the C2 methyl group should mitigate this type of reactivity and allow for isolation of the corresponding 1,2-addition product. This hypothesis was validated when, upon treatment of sulfinimine **96c** with Grignard reagent **216** followed by in situ methylation, sulfinamide **217** was isolated in 68% yield as a single diastereomer.

Sulfinamide **217** was elaborated to dihydroindolone **207** following our optimized three-step protocol for pyrrolidine formation. Thus, Pd-catalyzed cross-coupling of

sulfinamide **217** with stannane **105** proceeded smoothly to give enol ether **218**. Acid-mediated cyclization furnished an enamine intermediate, which was then selectively reduced to afford dihydroindolone **207** in 61% yield over three steps.

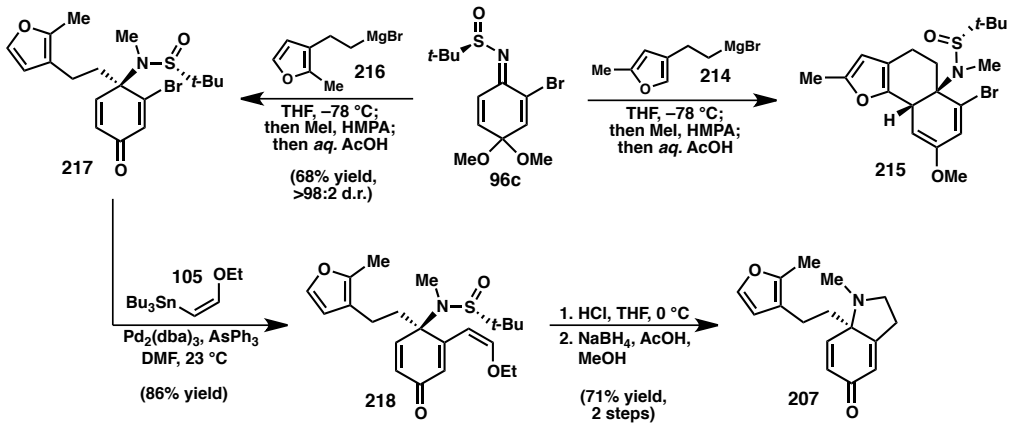


Figure 6. Preparation of a [2+2] cycloaddition substrate.

4.3.3. Evaluation of a Photo [2+2] Cycloaddition. With **207** hand, we were poised to study the key photochemical [2+2] cycloaddition reaction to establish the propellane core of acutumine. While we were confident we could obtain the desired linear [2+2] product, it was also noted we could generate the analogous crossed product, in which the cycloaddition occurs across the other face of the furan olefin (Figure 7, **206** versus **219**). Further, it was evident that issues of chemoselectivity might arise, given the different combinations of potential [2+2] coupling partners (e.g., formation of **220**).

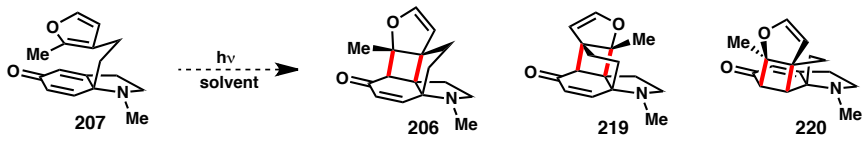


Figure 7. Possible products from photo [2+2] cycloaddition of **207**.

We nevertheless conducted a screen of photochemical reaction conditions, varying both the solvent and the irradiation wavelength.[6] Irradiation of **207** at 350 nm in benzene afforded trace amounts of the desired [2+2] product as determined by ^{1}H NMR analysis. However, following characterization by NMR and IR spectroscopy and HRMS, the major product of this reaction was assigned as diketone **223** (Figure 8). Diketone **223** is hypothesized to arise by a photolytic oxa-di-π-methane rearrangement,[7] which, following C–C bond fragmentation, generates the unstable iminium ion **222**. Nucleophilic addition of adventitious water results in iminium hydrolysis and intramolecular conjugate addition to produce **223**.

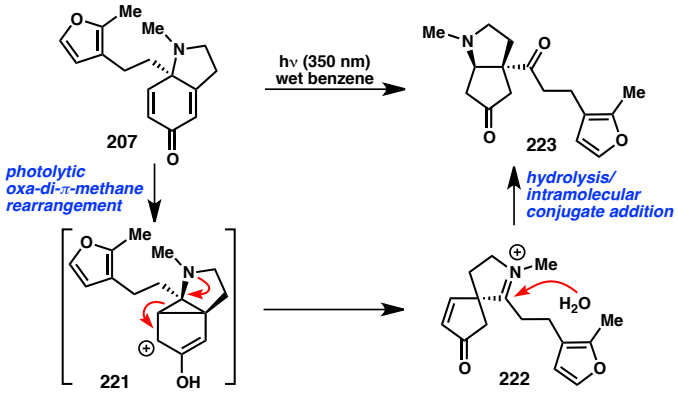


Figure 8. [2+2] photocycloaddition of dihydroindolone **207**.

To circumvent this type of undesired reactivity, the C7-C8 enone functionality was masked as its epoxide under nucleophilic epoxidation conditions (Figure 9). We were pleased to find that photochemical [2+2] cycloaddition of enone **224** proved more fruitful: a brief screen of reaction parameters revealed that irradiation of **224** at 350 nm in pentane was optimal, delivering dihydrofuran **225** in 72% yield. Notably, this reaction

exhibits a high degree of regioselectivity (for the linear vs. crossed product) and installs the vicinal all-carbon quaternary centers of acutumine in a single step.

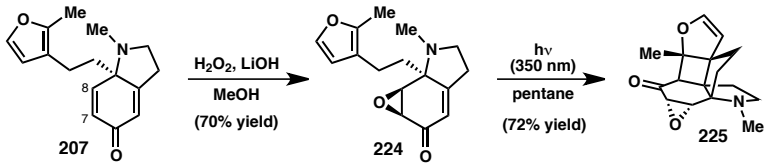


Figure 9. Photocycloaddition of epoxyenone **224**.

4.3.4. Examination of a Retro-Aldol/Aldol Reaction. Having successfully prepared the propellane core of acutumine, attention turned to investigating the second key retrosynthetic disconnection: the retro-aldol/aldol sequence. In particular, we anticipated that oxidation of dihydrofuran **225** would initially generate lactol **226** (Figure 10). At the outset of these studies, it was unclear if this lactol would be an isolable intermediate. Given the strain embedded within the cyclobutane moiety, it was hypothesized that C–C bond scission would be facile and may even occur under the oxidation conditions to deliver aldehyde **227**. Exposure of **227** to acidic or basic conditions was then expected to facilitate intramolecular aldol reaction to afford spirocyclic cyclopentanone **229**.

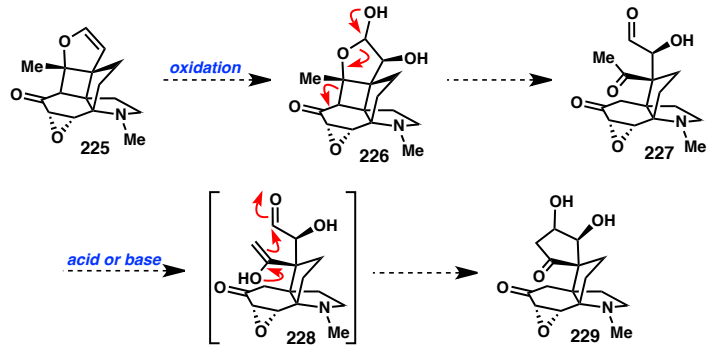


Figure 10. A retro-aldol/adol strategy for cyclopentenone synthesis.

We first examined the conversion of the dihydrofuran to a lactol-containing substrate using standard electrophilic epoxidation conditions. Whereas exposure of **225** to dimethyldioxirane, *m*-chloroperoxybenzoic acid, or simple oxaziridines led to *N*-oxidation, treatment with *N*-bromosuccinimide in aqueous THF[8] afforded bromohydrin **230** in excellent yield as a ~3:1 mixture of diastereomers at the lactol carbon (Figure 11). The bromohydrin proved to be a surprisingly stable intermediate that could be easily purified by silica gel chromatography. Single-crystal X-ray diffraction of **230** confirmed the regiochemical outcome of the photocycloaddition, which generates the linear [2+2] product. To our dismay, attempts to facilitate a retro-aldol fragmentation of **230** under mildly acidic or basic conditions led to significant decomposition and failed to produce detectable quantities of **232** or similar fragmentation products.

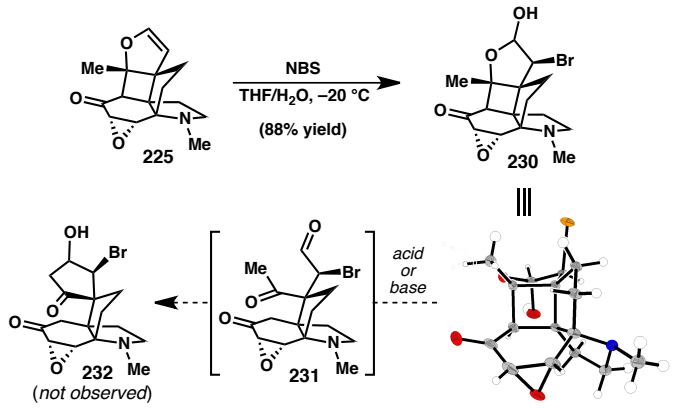


Figure 11. Attempted fragmentation of bromohydrin **230**.

In light of these results, we suspected that the epoxide moiety of **230** might be a source of undesired reactivity under our retro-aldol conditions. Thus, attention turned to the construction of dihydrofuran **234**, an intermediate in which the C7-C8 alkene has

been reduced (Figure 12). To this end, Cu-catalyzed conjugate reduction of **207** furnished enone **233**, a substrate that performed well under the previously optimized photo [2+2] reaction conditions to give dihydrofuran **234** in 71% yield. After an extensive screen of oxidation conditions, dihydrofuran **234** was found to undergo dihydroxylation under Upjohn conditions[9] to provide diol **235** in good yield. Like its bromohydrin analog, **235** proved to be remarkably stable to silica gel chromatography.

With access to lactol **235**, a number of conditions were evaluated for their ability to cleave the C4-C5 bond by a retro-aldol reaction. Unfortunately, as was observed with bromohydrin **230**, a variety of acidic or basic conditions failed to deliver the desired product. However, a benzene stock solution of diol **235** used for TLC analysis was found to slowly develop a single, new spot over the course of several days. To our surprise, isolation and single-crystal X-ray diffraction of this compound identified it as hemiketal **238**.

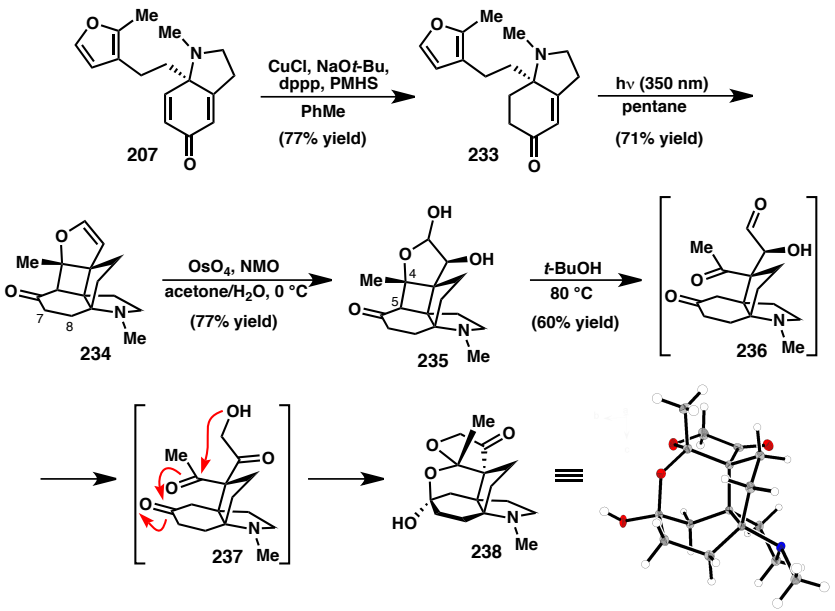


Figure 12. Isolation of ketal rearrangement product **238**.

It is proposed that aldehyde **236**, the product directly formed by retro-aldol fragmentation of **235**, readily tautomerizes to keto-alcohol **237**. Formation of this primary alcohol triggers an intramolecular cyclization cascade, leading to hemiketal **238**. A brief solvent screen identified *t*-BuOH as the optimal solvent for this rearrangement, which could be achieved in 60% yield when the reaction mixture was heated to 80 °C. Ketal **238** has thus far proven recalcitrant in our efforts toward further elaboration to **133**. Nevertheless, the isolation of **238** confirmed the viability of the [2+2] cycloaddition/retro-aldol sequence to prepare the aza-propellane core of acutumine.

4.3.5. A Lactone Fragmentation Strategy. Given the intermediacy of retro-aldol product **236**, we next sought to access an isolable cyclobutane fragmentation intermediate that could be advanced to the natural product. Specifically, it was envisioned that a deleterious tautomerization/ketalization event would be precluded in the corresponding lactone substrate (**239**, Figure 13). Indeed, nucleophilic ring opening of lactone **239** would deliver α-hydroxyester **240**, an intermediate without an accessible tautomerization pathway. Moreover, a Dieckmann cyclization between the methyl ketone and ester moieties of **240** would deliver an acutumine precursor (**241**) bearing the appropriate oxidation pattern about its cyclopentenone ring.

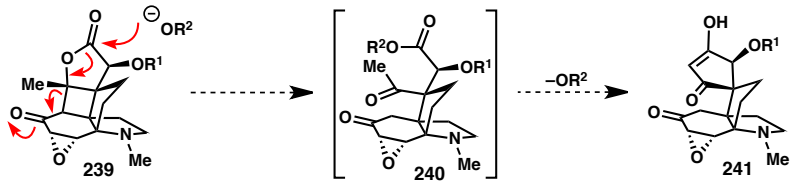


Figure 13. A retro-Dieckmann/retro-aldol approach.

The preparation of a suitable lactone substrate commenced with dihydrofuran **225** (Figure 14). Exposure of **225** to the previously identified dihydroxylation conditions delivered lactol **242** as an inconsequential 3:1 mixture of diastereomers. A screen of numerous oxidation conditions revealed that treatment with chromic acid was optimal, generating lactone **243** in 60% yield over 2 steps. Remarkably, **243** is the exclusive oxidation product formed in this reaction. At this point, we sought to protect the free alcohol of **243** as its benzyl ether; however, reaction of **243** with Cs_2CO_3 and benzyl bromide[10] (BnBr) did not afford the desired product. Instead, 1 and 2D NMR analysis identified the major product as cyclobutane **245**, which was obtained in 40% yield. It is hypothesized that this unusual product results from an initial base-mediated elimination of the lactone to deliver carboxylate anion **244**. This intermediate then reacts with BnBr and undergoes olefin isomerization to produce **245**.

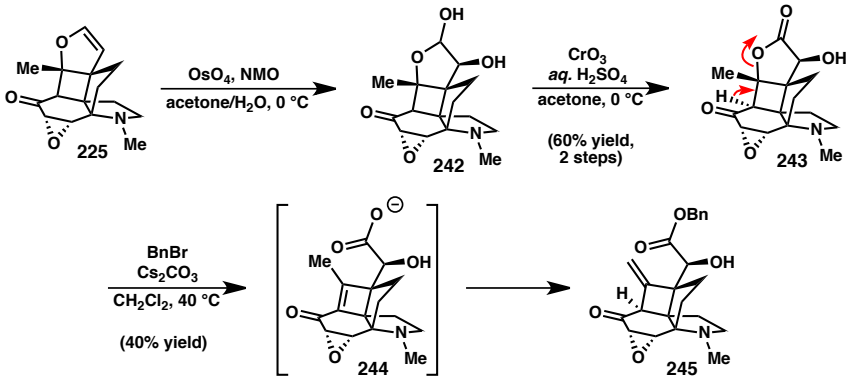


Figure 14. Isolation of cyclobutane **245**.

To mitigate the reactivity of the cyclobutane moiety, the use of more mild protection conditions was examined. To our delight, exposure of lactone **243** to TBSCl and *i*Pr_2NEt in refluxing CH_2Cl_2 furnished silyl ether **246** in 66% yield (Figure 15). With **246** in hand,

a nucleophile-mediated lactone opening/fragmentation reaction of **246** was investigated. Unfortunately, addition of numerous alcohol, amine, and thiol nucleophiles to **246** failed to give the desired product; under most reaction conditions, a complex mixture of products was observed. Interestingly, treatment of lactone **246** with K_2CO_3 in MeOH cleanly afforded a single product by ^{1}H NMR. Isolation and extensive 2D NMR characterization revealed the product to be ketal **248**. It is proposed that methanolysis of **246** generates epoxyketone **247**, which reacts further in a methoxide-mediated cyclization cascade to provide the observed ketal product.[11]

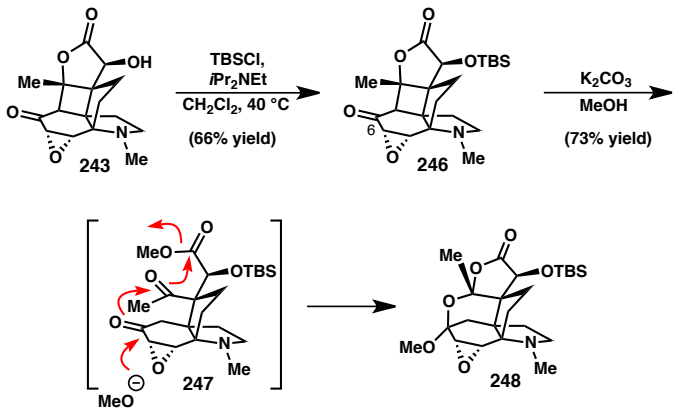


Figure 15. Fragmentation of lactone **246**.

The formation of **248** is not unlike the rearrangement observed in the retro-aldol fragmentation of **235** (see Figure 12): in both transformations, the electrophilicity of the C6 ketone enables the formation of thermodynamically stable ketal products. Moving forward, it was hypothesized that preparation of a lactone substrate bearing a tethered nucleophile could facilitate the desired fragmentation reaction under more mild reaction conditions, thereby attenuating the reactivity of the resulting epoxyketone intermediate.

To this end, carbamate **249** was prepared by exposure of **243** to ethyl isocyanate and DMAP in MeCN (Figure 16). We were pleased to find that addition of K_2CO_3 to a solution of **249** in MeOH generates the carbamate anion, which triggers a lactone opening/retro-aldol sequence to initially deliver diketone **251**; unfortunately, this intermediate readily undergoes intramolecular aldol ring closure to produce **252** in 75% yield.

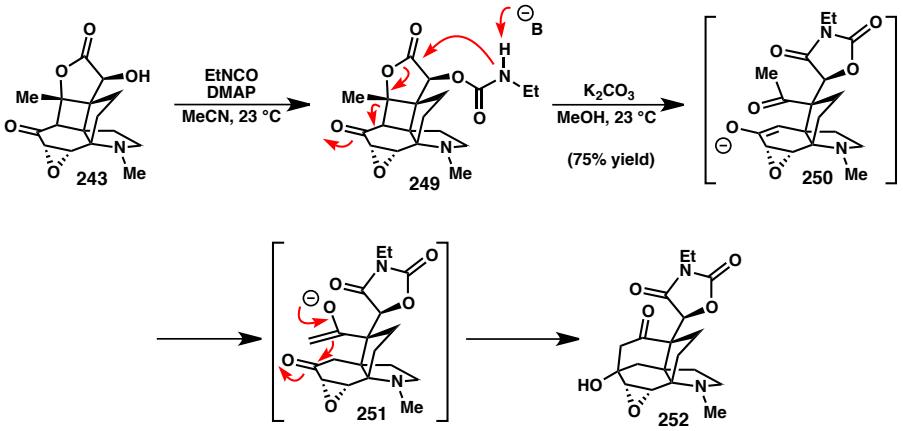


Figure 16. Functionalization of carbamate-tethered lactone **249**.

Taken collectively, our attempts to prepare the cyclopentenone of acutumine via base-mediated cyclization reactions illustrate that the C6 ketone is too reactive under a number of conditions. To circumvent these challenges, we examined a one-pot fragmentation/silylation of **249** in which the transiently formed enolate (**250**) could be trapped as its silyl ether. To our delight, exposure of **249** to LiHMDS followed by addition of HMPA and TBSOTf at –78 °C afforded silyl enol ether **253** in 63% yield (Figure 17). With Dieckmann cyclization precursor **253** in hand, a small screen of reaction parameters was conducted. Under carefully optimized conditions, methyl ketone

253 could be converted to spirocycle **254** using 1.1 equivalents of KO*t*-Bu in THF at –20 °C. Notably, **254** possesses the carbocyclic core of acutumine and presents appropriate functional handles to elaborate to the natural product.

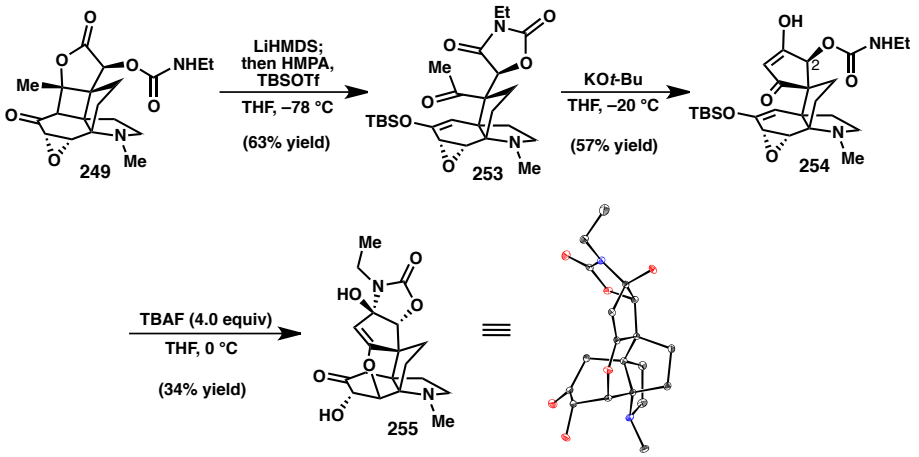


Figure 17. Construction of the carbocyclic core of acutumine.

Spirocycle **254** represents our most advanced intermediate in our synthesic efforts toward acutumine. While we were pleased with our ability to access the acutumine framework, we sought to corroborate our structural assignment by X-ray analysis of a cyclopentenone-containing intermediate. Toward this goal, treatment of **254** with excess TBAF afforded a new, crystalline solid in 34% yield. Single crystal X-ray diffraction of this compound confirmed the formation of hexacyclic aminal **255**. In addition to undergoing the desired desilylation reaction, this peculiar product results from (1) intramolecular epoxide opening by the enol of the cyclopentenone, (2) epimerization of the C2 carbinol, and (3) cyclization of the carbamate onto the enone carbonyl. Although this type reactivity was not expected, the formation of **255** ultimately presents a potential

avenue by which to elaborate the epoxide of **254** to the dimethoxyenone of the natural product.

4.4. Future Directions

Having prepared spirocycle **254**, our immediate objective is to advance this intermediate to dechloroacutumine (**134**, Figure 18). As such, exposure of enol ether **249** to mild methylation conditions should deliver methoxyenone **256**. Oxidative epoxide opening[12] of this intermediate should give an α-hydroxy ketone, which upon exhaustive methylation is expected to yield diene **257**. Finally, desilyation and deprotection of the carbamate should deliver **134**.

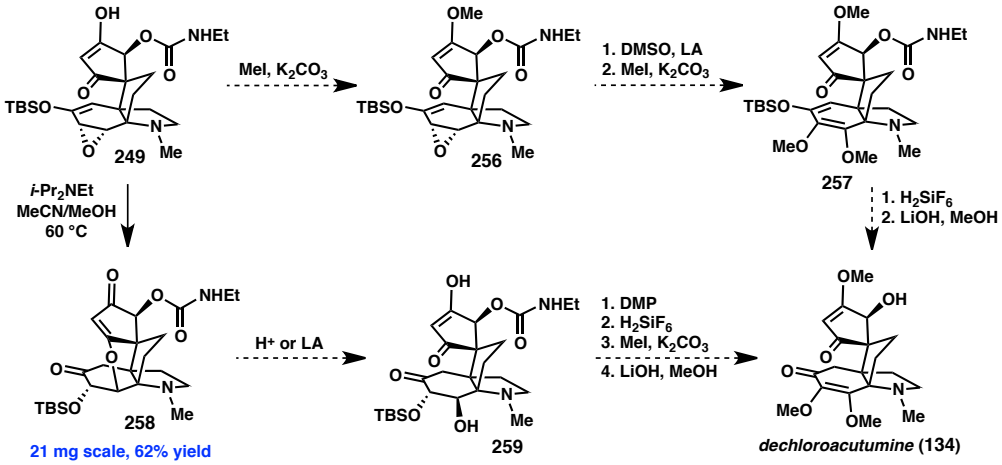


Figure 18. Proposed end-game strategy for dechloroacutumine.

In the event this synthetic route proves unsuccessful, we envision pursuing an alternative strategy that takes advantage of the reactivity observed in the formation of **255** (see Figure 17). Specifically, preliminary studies have demonstrated that exposure of **249** to *i*-Pr$_2$NEt in MeCN/MeOH at 60 °C facilitates an intramolecular epoxide opening

reaction to give pentacycle **258** in 56% isolated yield (Figure 18). To advance this intermediate to **134**, Brønsted or Lewis acid-mediated hydrolysis of the enol ether will furnish alcohol **259**. This intermediate can undergo an oxidation/desilylation/methylation sequence to install the dimethoxyenone, followed by carbamate deprotection to yield the natural product.

In accord with the long-term goals of this project, we also plan to thoroughly investigate installation of the stereogenic chloride. While our preliminary studies regarding an early-stage C–Cl bond formation were not fruitful, we have begun to pursue alternative [2+2] substrates using the enolate 1,2-addition protocol described in section 4.3.1. Alternatively, we are poised to exploit the carbamate functionality of **249** to implement a directed, late-stage C–H activation reaction for chloride installation.[13] In this regard, our synthesis is amenable to the preparation of a number of directing group-bearing substrates from the divergent functionalization of lactone **243**.

4.5. Concluding Remarks

In summary, we have developed a synthesis of the carbocyclic framework of acutumine in only 12 steps from commercially available starting materials. Key to the success of our approach is a photochemical [2+2] cycloaddition to install the vicinal all-carbon quaternary stereocenters and a lactone fragmentation/Dieckmann cyclization sequence to construct the spirocyclic cyclopentenone. These investigations were ultimately enabled by the versatility of our highly diastereoselective 1,2-addition reaction. Notably, by changing the nature of the nucleophile employed, we have the power to explore a number of different strategies en route to acutumine. We are confident

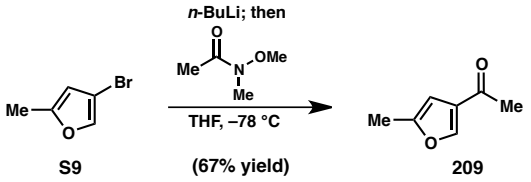
the studies discussed above will lead to the construction of more appropriately oxidized propellane intermediates, which will facilitate our synthetic endeavors towards the completion of the natural product.

4.6. Experimental Section

4.6.1. Materials and Methods. Unless otherwise stated, reactions were performed under a nitrogen atmosphere using freshly dried solvents. Tetrahydrofuran (THF), methylene chloride (CH_2Cl_2), diethyl ether (Et_2O), acetonitrile (MeCN), and toluene (PhMe) were dried by passing through activated alumina columns. MeOH was distilled over magnesium oxide and triethylamine (Et_3N) was distilled over calcium hydride prior to use. Unless otherwise stated, chemicals and reagents were used as received. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 pre-coated plates (0.25 mm) and were visualized by UV, *p*-anisaldehyde, or $KMnO_4$ staining. Flash column chromatography was performed either as described by Still et al. (Still, W. C., Kahn, M.; Mitra, A. *J. Org. Chem*. **1978**, *43*, 2923-2925) using silica gel (partical size 0.032-0.063) purchased from Silicycle or using pre-packaged RediSep®Rf columns on a CombiFlash Rf system (Teledyne ISCO Inc.). Optical rotations were measured on a Jasco P-2000 polarimeter using a 100 mm path-length cell at 589 nm. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Inova 500 (at 500 MHz and 126 MHz, respectively) and are reported relative to internal $CHCl_3$ (^{1}H, δ = 7.26; ^{13}C, δ = 77.0). Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, app = apparent. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). HRMS were acquired using an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI), or mixed (MM) ionization mode. Melting points were determined using a Büchi B-545 capillary melting point apparatus and the values reported are uncorrected.

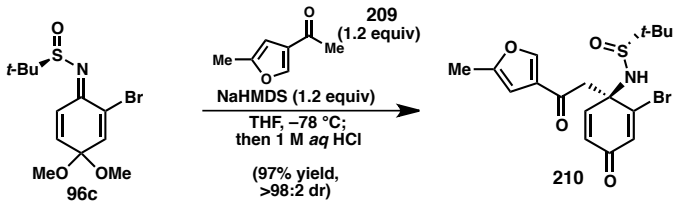
4.6.2. Procedures and Spectroscopic Data

Preparation of ketofuran 209.



To a solution of **S9**[14] (343 mg, 2.13 mmol) in THF (7 mL) at –78 °C was added *n*-BuLi (0.93 mL, 2.29 M solution in Hexanes, 2.13 mmol) dropwise by syringe. The resulting pale yellow solution was stirred 10 minutes at –78 °C, then *N*-methoxy-*N*-methylacetamide (226 μL, 2.13 mmol) was added dropwise by syringe. The reaction was allowed to stir at –78 °C for 2 hours, then quenched by the addition of a solution of AcOH (150 μL) in Et_2O (5 mL). The reaction was removed from the –78 °C bath, water (4 mL) was added, and was allowed to warm to room temperature. The organic layer was washed with with water (2 x 5 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure, *being careful to keep the pressure above ~120 torr*. The crude material was purified by flash chromatography (10 to 20% Et_2O in Pentane) to afford ketofuran **209** (178 mg, 67% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (s, 1H), 6.33 (t, J = 1.0 Hz, 1H), 2.38 (s, 3H), 2.29 (d, J = 1.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.7, 154.3, 146.2, 128.9, 104.2, 27.52, 13.37. FTIR (NaCl, thin film) 3127, 2925, 1678, 1544, 1395, 1354, 1296, 1142, 936, 910, 824 cm^{-1}.

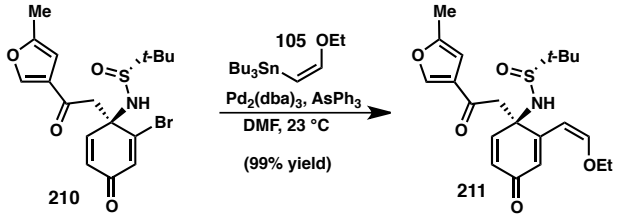
Preparation of sulfinamide 210.



To a solution of **209** (247 mg, 1.99 mmol) in THF (6 mL) at –78 °C was added a solution of NaHMDS (0.9 M solution in THF, 2.2 mL, 2.0 mmol) dropwise by syringe. The reaction was allowed to stir 1 hour at –78 °C, then a solution of **96b** (558 mg, 1.66 mmol) in THF (1 mL) was added dropwise by syringe. The resulting orange solution was stirred at –78 °C for 3 hours, then quenched by the addition of 1 N HCl (8 mL). The

reaction was warmed to room temperature and stirred vigorously for 20 minutes. The reaction mixture was diluted with EtOAc (30 mL) and washed with saturated aqueous $NaHCO_3$ (10 mL). The aqueous layer was extracted with EtOAc (10 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a tan oil. The diastereoselectivity was determined to be >98:2 by ^{1}H NMR. Flash chromatography (40% to 60% EtOAc in Hexanes) afforded sulfinamide **210** (667 mg, 97% yield) as a pale yellow foam. $[\alpha]_D^{25}$ –92.3° (*c* 0.88, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 1.0 Hz, 1H), 7.38 (d, *J* = 10.1 Hz, 1H), 6.85 (d, *J* = 1.8 Hz, 1H), 6.33 (t, *J* = 1.1 Hz, 1H), 6.30 (dd, *J* = 10.1, 1.8 Hz, 1H), 5.99 (s, 1H), 3.47 (d, *J* = 16.2 Hz, 1H), 2.93 (d, *J* = 16.2 Hz, 1H), 2.31 (d, *J* = 1.1 Hz, 3H), 1.29 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.3, 182.8, 155.3, 150.5, 148.5, 147.1, 135.7, 128.5, 126.7, 103.9, 60.6, 57.1, 47.5, 22.7, 13.4. FTIR (NaCl, thin film) 3246, 2960, 2924, 1670, 1599, 1543, 1293, 1144, 1070, 956, 910, 731 cm^{-1}; HRMS (ESI+) calc'd for $C_{17}H_{20}NO_4SBr$ $[M+H]^+$ 416.0369, found 416.0373.

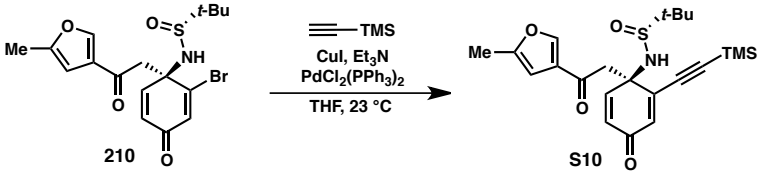
Preparation of enol ether 211.



To a solution of sulfinamide **210** (100 mg, 0.24 mmol) in DMF (2.4 mL) was added $Pd_2(dba)_3$ (11 mg, 0.012 mmol), $AsPh_3$ (15 mg, 0.048 mmol) and stannane **105** (0.089 mL, 0.27 mmol). The solution was degassed with N_2 for 30 minutes, then stirred at room temperature for an additional 30 minutes. The solution was passed through a short plug of Celite, diluted with EtOAc (20 mL), and washed with H_2O (3 x 10 mL). The combined aqueous layers were back extracted with EtOAc (20 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford a brown oil. Flash chromatography (50% to 75% EtOAc in Hexanes) gave enol ether **211** (97 mg, 99% yield) as an inseparable mixture of >1:10 E/Z isomers. $[\alpha]_D^{25}$ –93.0° (*c* 0.91, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 0.9 Hz, 1H), 7.18–7.13 (m, 2H), 6.58 (d, *J* = 7.2 Hz, 1H), 6.31 (t, *J* = 1.0 Hz, 1H), 6.22 (dd, *J* = 10.2, 2.0 Hz,

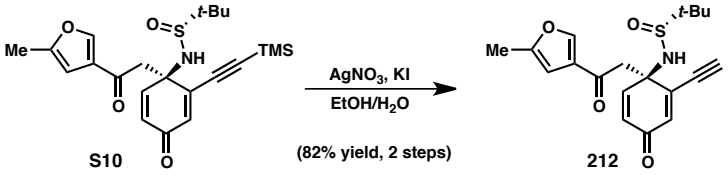
1H), 5.94 (s, 1H), 5.05 (d, J = 7.2 Hz, 1H), 4.12–4.00 (m, 2H), 3.13 (d, J = 16.1 Hz, 1H), 2.85 (d, J = 16.0 Hz, 1H), 2.29 (d, J = 1.1 Hz, 3H), 1.37 (t, J = 7.1 Hz, 3H), 1.25 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.6, 186.2, 155.1, 154.1, 152.2, 150.1, 147.1, 128.7, 127.6, 127.4, 104.0, 99.4, 70.8, 58.3, 56.4, 48.3, 22.7, 15.4, 13.4. FTIR (NaCl, thin film) 3245, 2979, 2926, 1654, 1624, 1577, 1543, 1388, 1326, 1290, 1144, 1101, 1058, 911, 897, 731 cm^{-1}; HRMS (ESI+) calc'd for $C_{21}H_{27}NO_5S$ $[M+H]^+$ 406.1683, found 406.1682.

Preparation of enyne S10.



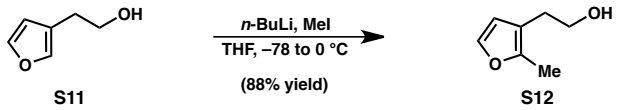
A round bottom flask was charged with sulfinamide **210** (300 mg, 0.724 mmol), $PdCl_2(PPh_3)_2$ (25 mg, 0.036 mmol), CuI (6.9 mg, 0.036 mmol), and THF (3.5 mL). The resulting yellow solution was degassed with N_2 for 20 minutes. Then, Et_3N (3.5 mL) and ethynyltrimethylsilane (113 μL, 0.797 mmol) were sequentially added, and the reaction mixture was allowed to stir 1 hour at room temperature. The mixture was filtered through Celite, rinsed with EtOAc, and concentrated under reduced pressure to give a yellow oil. The crude product was used in the following step without further purification. A small sample was purified by flash chromatography (40 to 75% EtOAc in Hexanes) for characterization purposes: $[\alpha]_D^{25}$ –61.3° (*c* 0.72, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.20 (d, J = 10.3 Hz, 1H), 6.56 (d, J = 2.0 Hz, 1H), 6.33 (s, 1H), 6.26 (dd, J = 10.3, 2.0 Hz, 1H), 5.84 (s, 1H), 3.41 (d, J = 16.1 Hz, 1H), 2.95 (d, J = 16.1 Hz, 1H), 2.31 (s, 3H), 1.26 (s, 9H), 0.21 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.8, 184.4, 155.2, 150.5, 147.1, 141.6, 135.3, 128.7, 127.6, 108.1, 104.0, 100.5, 58.3, 56.6, 47.6, 22.7, 13.4, -0.5. FTIR (NaCl, thin film) 3245, 2959, 1661, 1544, 1390, 1311, 1251, 1144, 1068, 897, 847, 761 cm^{-1}; HRMS (ESI+) calc'd for $C_{22}H_{29}NO_4SiS$ $[M+H]^+$ 432.1659, found 432.1664.

Preparation of enyne 212.



To a solution of **S10** (0.724 mmol) in EtOH (48 mL) and H_2O (12 mL) was added $AgNO_3$ (148 mg, 0.869 mmol). The reaction was allowed to stir for 3 hours, then KI (156 mg, 0.941 mmol) was added, and the reaction was stirred for an additional 30 minutes. The resulting mixture was filtered through Celite, rinsed with EtOAc, concentrated under reduced pressure, and purified by flash chromatography (50 to 75% EtOAc in Hexanes) to afford enyne **212** (213 mg, 82% yield) as pale brown solid. $[\alpha]_D^{25}$ –84.2° (*c* 0.89, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 1.0 Hz, 1H), 7.25 (d, *J* = 10.3 Hz, 1H), 6.62 (d, *J* = 1.9 Hz, 1H), 6.33 (t, *J* = 1.0 Hz, 1H), 6.28 (dd, *J* = 10.3, 2.0 Hz, 1H), 5.86 (s, 1H), 3.54 (d, *J* = 0.6 Hz, 1H), 3.47 (d, *J* = 16.3 Hz, 1H), 2.97 (d, *J* = 16.3 Hz, 1H), 2.31 (d, *J* = 1.1 Hz, 3H), 1.26 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.5, 184.1, 155.2, 150.7, 147.0, 140.8, 136.16, 128.5, 127.5, 103.9, 88.9, 79.7, 58.3, 56.7, 47.4, 22.6, 13.4. FTIR (NaCl, thin film) 3246, 2961, 2093, 1662, 1624, 1543, 1391, 1313, 1287, 1144, 1063, 909, 731 cm^{-1}; HRMS (ESI+) calc'd for $C_{19}H_{21}NO_4S$ $[M+H]^+$ 360.1264, found 360.1262.

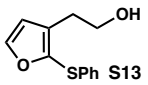
Synthesis of furanyl alcohols:



Preparation of alcohol S12. To a solution of 2-(3-furanyl)ethanol[15] (**S11**) (1.85 g, 16.5 mmol) in THF (80 mL) at –78 °C was added *n*-BuLi (2.32 M solution in Hexanes, 14.2 mL, 33.0 mmol) dropwise by syringe, and the resulting solution was allowed to stir at –78 °C for 30 minutes. Upon warming to 0 °C and stirring an additional 30 minutes, MeI (2.1 mL, 33.0 mmol) was added dropwise by syringe. The reaction mixture was allowed to stir 1 hour at 0 °C, then quenched by the addition of H_2O (30 mL) and extracted with Et_2O (3 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered, concentrated under reduced pressure, and purified by flash chromatography

(25% EtOAc in Hexanes) to afford alcohol **S12** (1.83 g, 88% yield) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 1.4 Hz, 1H), 6.22 (d, *J* = 1.2 Hz, 1H), 3.74 (t, *J* = 6.5 Hz, 2H), 2.60 (t, *J* = 6.5 Hz, 2H), 2.24 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.7, 140.2, 114.9, 111.4, 62.7, 28.3, 11.5; FTIR (NaCl, thin film) 3400, 2921, 1740, 1512, 1374, 1202, 1166, 1129, 1046, 939, 893, 731 cm^{-1}; HRMS (ESI+) calc'd for $C_7H_{10}O_2$ $[M+H]^+$ 126.0681, found 126.0649.

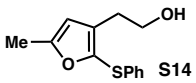
Preparation of furanyl alcohol S13.



S13

Prepared from 8.92 mmol of 2-(3-furanyl)ethanol (**S11**) using the above general procedure with diphenyl disulfide (3.89 g, 17.8 mmol) as the electrophile (added in one solid portion). The crude product was purified by flash chromatography (25% EtOAc in Hexanes) to give alcohol **S13** (1.78 g, 75% yield) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 2.0 Hz, 1H), 7.28–7.21 (m, 2H), 7.21–7.11 (m, 1H), 7.14–7.06 (m, 2H), 6.50 (d, *J* = 2.0 Hz, 1H), 3.78 (t, *J* = 6.5 Hz, 2H), 2.81 (t, *J* = 6.5 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.9, 140.1, 136.7, 130.2, 129.1, 126.9, 126.1, 112.9, 62.4, 29.3; FTIR (NaCl, thin film) 3338, 2947, 2879, 1582, 1478, 1440, 1142, 1067, 1024, 890, 738 cm^{-1}; HRMS (ESI+) calc'd for $C_{12}H_{12}O_2S$ $[M+H]^+$ 221.0631, found 221.0627.

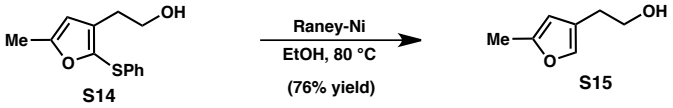
Preparation of furanyl alcohol S14.



S14

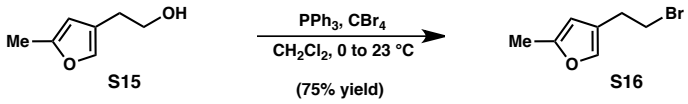
Prepared from 6.81 mmol of alcohol **S13** using the above general procedure. The crude product was purified by flash chromatography (25% EtOAc in Hexanes) to give alcohol **S14** (1.43 g, 89% yield) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 – 7.21 (m, 2H), 7.17 – 7.12 (m, 1H), 7.12 – 7.07 (m, 2H), 6.11 (d, *J* = 1.1 Hz, 1H), 3.76 (q, *J* = 6.2 Hz, 2H), 2.75 (t, *J* = 6.5 Hz, 2H), 2.32 (d, *J* = 1.0 Hz, 3H), 1.42 (t, *J* = 5.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.2, 137.34, 137.33, 131.8, 129.0, 126.50, 125.9, 109.3, 62.5, 29.4, 14.1. FTIR (NaCl, thin film) 3338, 2947, 2923, 2878, 1605, 1583, 1478, 1440, 1248, 1116, 1048, 1024, 956, 808, 739 cm^{-1}; HRMS (ESI+) calc'd for $C_{13}H_{14}O_2S$ $[M+H]^+$ 235.0787, found 235.0791.

Preparation of furanyl alcohol S15.



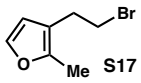
To a solution of furanyl alcohol **S14** (775 mg, 3.31 mmol) in EtOH (50 mL) was added Raney-Ni (1.50 g, 200 wt %), and the resulting suspension was heated to 80 °C. The reaction was allowed to stir a total of 2 hours and 30 minutes at 80 °C, adding additional portions of Raney-Ni (1.50 g, 200 wt %) every 30 minutes (for a total of 6 g Raney-Ni). The reaction was cooled to room temperature, filtered through a pad of Celite®, and concentrated under reduced pressure. The crude residue was purified by flash chromatography (25% EtOAc in Hexanes) to provide alcohol **S15** (319 mg, 76% yield) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (d, J = 1.0 Hz, 1H), 5.90 (t, J = 1.1 Hz, 1H), 3.75 (t, J = 6.3 Hz, 2H), 2.62 (td, J = 6.4, 0.9 Hz, 2H), 2.26 (d, J = 1.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.7, 138.0, 122.0, 107.0, 62.4, 28.4, 13.5. FTIR (NaCl, thin film) 3367, 2922, 2880, 1617, 1554, 1448, 1383, 1266, 1119, 1050, 1021, 920, 805 cm^{-1}; HRMS (ESI+) calc'd for $C_7H_{10}O_2$ $[M+H]^+$ 126.0681, found 126.0635.

Synthesis of furanyl bromide substrates:



Preparation of bromide S16. To a solution of alcohol **S15** (318 mg, 2.52 mmol) and CBr_4 (1.00 g, 3.02 mmol) in CH_2Cl_2 (11 mL) at 0 °C was added PPh_3 (793 mg, 3.02 mmol) in one portion. The resulting solution was allowed to stir at 0 °C for 5 minutes, then warmed to room temperature and stirred an additional 30 minutes. The reaction mixture was dry loaded onto silica gel (6 g) and purified by flash chromatography (0 to 2% Et_2O in Hexanes) to give bromide **S16** (360 mg, 75% yield) as a colorless oil. Bromide **S6** is a fairly unstable intermediate and was immediately converted to its Grignard reagent upon preparation.

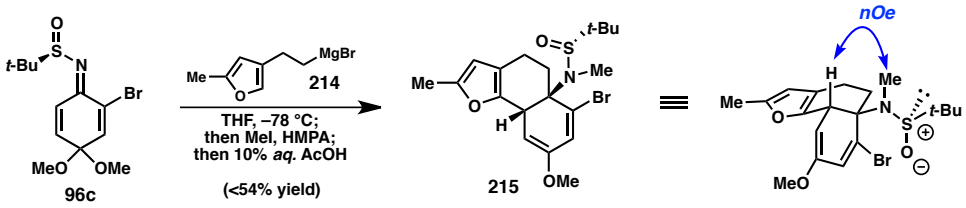
Preparation of bromide S17.



Prepared from 14.5 mmol alcohol **S12** using the above general procedure. The reaction mixture was dry loaded onto silica gel (40 g) and purified by flash chromatography (0 to 2% Et_2O in Hexanes) to give bromide **S17** (1.91

g, 70% yield) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 1.9 Hz, 1H), 6.23 (d, *J* = 1.9 Hz, 1H), 3.46 (t, *J* = 7.5 Hz, 2H), 2.91 (t, *J* = 7.5 Hz, 2H), 2.24 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.5, 140.2, 116.2, 111.0, 32.6, 28.9, 11.5. FTIR (NaCl, thin film) 2922, 2860, 1624, 1513, 1449, 1437, 1281, 1224, 1156, 1135, 939, 893, 731 cm^{-1}; HRMS (ESI+) calc'd for C_7H_9OBr $[M+H]^+$ 187.9837, found 187.9830.

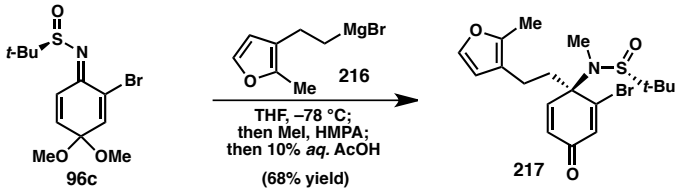
Preparation of enol ether 215.



To a solution of sulfinimine **96c** (71 mg, 0.21 mmol) in THF (0.4 mL) at –78 °C was added a solution of Grignard reagent **214** (0.5 M solution in THF, 0.47 mL, 0.23 mmol)[16] dropwise by syringe. The resulting solution was then stirred at –78 °C for 1 hour, then MeI (39 μL, 0.63 mmol) and HMPA (110 μL, 0.63 mmol) were sequentially added dropwise by syringe, and the solution stirred at –78 °C for ten minutes. The reaction was then warmed to 23 °C and stirred for 12 hours, then quenched by the addition of aqueous AcOH (10% v/v, 0.8 mL). After 3 hours, the mixture was diluted with EtOAc (10 mL) and washed with H_2O (3 x 4 mL). The aqueous layer was back extracted with EtOAc (10 mL), and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (5 mL), dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by flash chromatography (25% to 60% EtOAc in Hexanes) to afford tricycle **215** (49 mg, 54% yield) as a pale yellow foam. The purified intermediate co-eluted with ~10% of an unidentified impurity. A small sample was further purified by preparative TLC (40% EtOAc in Hexanes) for characterization purposes: $[\alpha]_D^{25}$ +431.4° (c = 0.40, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.44 (d, *J* = 2.1 Hz, 1H), 5.75 (d, *J* = 1.1 Hz, 1H), 5.12 (dd, *J* = 6.2, 2.2 Hz, 1H), 3.82 (d, *J* = 6.2 Hz, 1H), 3.56 (s, 3H), 2.64 (dt, *J* = 13.0, 4.0 Hz, 1H), 2.58 (s, 3H), 2.56–2.50 (m, 1H), 2.39 (dt, *J* = 16.2, 3.7 Hz, 1H), 2.22 (s, 3H), 2.03 (ddd, *J* = 12.9, 10.6, 5.1 Hz, 1H), 1.19 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.2, 150.9, 147.3, 132.0, 127.6, 116.6, 105.6, 93.8, 66.5, 59.0, 54.8, 39.2, 32.6, 26.4, 24.6, 19.0, 13.6; FTIR (NaCl, thin film) 2952, 2922, 2863, 1657, 1577, 1453, 1362, 1251, 1218,

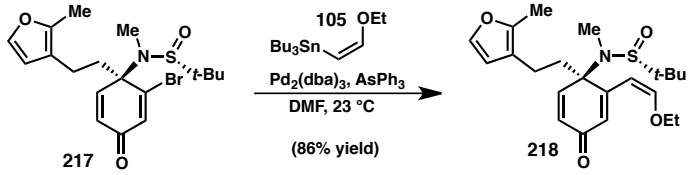
1175, 1072, 1024, 950, 806, 736 cm^{-1}; HRMS (ESI+) calc'd for $C_{19}H_{26}NO_3SBr$ $[M+H]^+$ 428.0897, found 428.0890.

Preparation of sulfinamide 217.



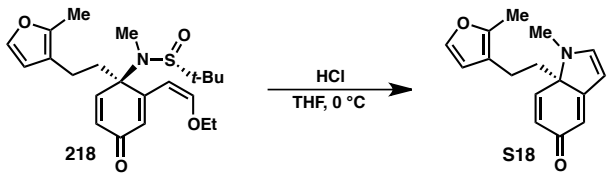
To a solution of sulfinimine **96c** (2.22 g, 6.60 mmol) in THF (13 mL) at –78 °C was added a solution of Grignard reagent **216** (0.64 M solution in THF, 12.4 mL, 7.92 mmol) dropwise by syringe. The solution was then stirred at –78 °C for 1 hour, then MeI (1.2 mL, 19 mmol) and HMPA (3.3 mL, 19 mmol) were sequentially added dropwise by syringe, and the solution stirred at –78 °C for 10 minutes. The solution was then warmed to 23 °C and stirred for 12 hours, then quenched by the addition of aqueous AcOH (10% v/v, 30 mL). After 3 hours, the mixture was diluted with Et_2O (40 mL) and washed with H_2O (3 x 20 mL). The aqueous layer was back extracted with Et_2O (50 mL), and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford a pale brown oil. The diastereoselectivity was determined to be >98:2 by ^1H NMR. Flash chromatography (20% to 60% EtOAc in Hexanes) afforded sulfinamide **217** as a pale yellow foam (1.76 g, 68% yield). $[\alpha]_D^{25}$ +6.4° (*c* 0.98, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.22 (d, *J* = 1.8 Hz, 1H), 6.93 (d, *J* = 1.8 Hz, 1H), 6.80 (d, *J* = 10.0 Hz, 1H), 6.44 (dd, *J* = 10.0, 1.8 Hz, 1H), 6.14 (d, *J* = 1.8 Hz, 1H), 2.71 (ddd, *J* = 12.9, 11.4, 5.6 Hz, 1H), 2.46 (s, 3H), 2.16 (s, 3H), 2.13–2.02 (m, 2H), 1.73 (ddd, *J* = 12.9, 11.6, 5.7 Hz, 1H), 1.23 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.1, 150.7, 150.0, 147.6, 140.2, 136.4, 129.7, 116.6, 111.1, 68.7, 59.2, 36.9, 26.7, 24.2, 19.5, 11.5; FTIR (NaCl, thin film) 2923, 1669, 1594, 1296, 1271, 1139, 1076, 949, 893 cm^{-1}; HRMS (ESI+) calc'd for $C_{18}H_{24}NO_3SBr$ $[M+H]^+$ 414.0733, found 414.0729.

Preparation of trienone 218.



To a solution of sulfinamide **218** (1.50 g, 3.61 mmol) in DMF (20 mL) was added $Pd_2(dba)_3$ (170 mg, 0.18 mmol), $AsPh_3$ (220 mg, 0.72 mmol) and stannane **105** (1.32 mL, 3.97 mmol). The solution was degassed with N_2 for 30 minutes, then stirred at room temperature for an additional 30 minutes. The solution was passed through a short plug of Celite, diluted with EtOAc (100 mL), and washed with H_2O (3 x 40 mL). The combined aqueous layers were back extracted with EtOAc (100 mL), and the organic layers were combined and dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford a brown oil. The product was obtained as a >10:1 mixture of *Z*:*E* olefin isomers. Flash chromatography (50% to 100% EtOAc in Hexanes) afforded enol ether **218** (1.26 g, 86% yield) as a tan foam. $[\alpha]_D^{25}$ –72.1° (c = 1.31, $CDCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (d, *J* = 1.9 Hz, 1H), 7.18 (d, *J* = 2.0 Hz, 1H), 6.60 (d, *J* = 7.2 Hz, 1H), 6.53 (d, *J* = 10.0 Hz, 1H), 6.36 (dd, *J* = 10.0, 2.0 Hz, 1H), 6.09 (d, *J* = 1.8 Hz, 1H), 5.15 (d, *J* = 7.2 Hz, 1H), 4.08–3.99 (m, 2H), 2.43 (s, 3H), 2.37 (ddd, *J* = 12.7, 11.2, 5.7 Hz, 1H), 2.10 (s, 3H), 2.09–2.03 (m, 2H), 1.75 (ddd, *J* = 12.6, 11.2, 5.8 Hz, 1H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.23 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.6, 154.7, 153.5, 149.4, 147.3, 139.9, 130.5, 128.9, 117.4, 111.2, 98.7, 70.7, 66.5, 58.9, 37.2, 27.1, 24.5, 24.4, 19.5, 15.4, 11.3; FTIR (NaCl, thin film) 2974, 2925, 1660, 1622, 1576, 1456, 1384, 1264, 1122, 1068, 954, 893 cm^{-1}; HRMS (ESI+) calc'd for $C_{22}H_{31}NO_4S$ $[M+H]^+$ 406.2047, found 406.2044.

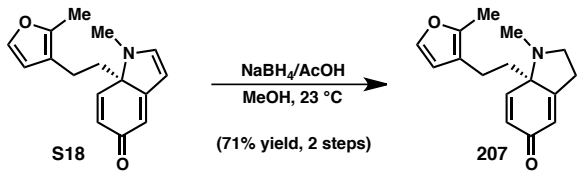
Preparation of enamine S18.



To a solution of enol ether **218** (778 mg, 1.92 mmol) in THF (38 mL) at 0 °C was added a solution of HCl (2.0 M solution in Et_2O, 19 mL, 38 mmol) dropwise by syringe over 1 minute. The reaction was allowed to stir an additional 2 minutes at 0 °C and

quenched by the addition of aqueous NaOH (10% w/v, 25 mL). The reaction was warmed to room temperature and stirred for an additional 5 minutes. The mixture was diluted with H_2O (10 mL) and extracted with EtOAc (3 x 40 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give crude enamine **S18** as a red oil, which was used immediately in the following step without further purification. A small sample was purified by flash chromatography (15 to 100% EtOAc in CH_2Cl_2) for characterization purposes: $[\alpha]_D^{25}$ –1847.5° (c = 0.63, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.15 (d, *J* = 1.8 Hz, 1H), 6.96 (dd, *J* = 9.8, 0.6 Hz, 1H), 6.88 (d, *J* = 3.3 Hz, 1H), 6.14 (dd, *J* = 9.8, 1.6 Hz, 1H), 6.05 (d, *J* = 1.8 Hz, 1H), 5.86 (d, *J* = 1.6 Hz, 1H), 5.45 (dd, *J* = 3.3, 0.4 Hz, 1H), 3.03 (s, *J* = 4.5 Hz, 3H), 2.20–2.07 (m, 2H), 2.11 (s, 3H), 1.96 – 1.89 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.7, 174.5, 153.4, 147.4, 140.0, 139.9, 131.1, 116.7, 111.1, 109.8, 99.6, 72.5, 44.2, 31.5, 18.5, 11.3. FTIR (NaCl, thin film) 2918, 1630, 1568, 1516, 1314, 1246, 1138, 1088, 1041, 884, 830 cm^{-1}; HRMS (ESI+) calc'd for $C_{16}H_{17}NO_2$ $[M+H]^+$ 256.1332, found 256.1332.

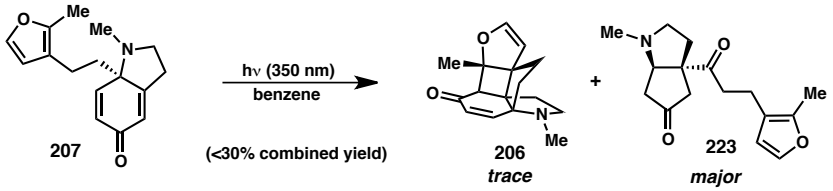
Preparation of dihydroindolone 207.



To a solution of crude enamine **S18** (1.92 mmol) in MeOH (38 mL) was added a premixed solution of $NaBH_4$ (145 mg, 3.84 mmol) in AcOH (13 mL), dropwise by syringe. The solution was stirred at room temperature for 1 hour, then another portion of $NaBH_4$ (145 mg, 3.84 mmol) in AcOH (13 mL) was added. After stirring an additional 30 minutes, the reaction was slowly poured into a solution of KOH (50% w/v, 60 mL) at 0 °C. The mixture was then diluted and extracted with EtOAc (3 x 60 mL). The combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by flash chromatography (50 to 100% EtOAc in CH_2Cl_2) to afford dihydroindolone **207** (349 mg, 71% yield, 2 steps) as a red oil. $[\alpha]_D^{25}$ +54.6° (c = 0.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.19 (d, *J* = 1.9 Hz, 1H), 6.95 (d, *J* = 10.0 Hz, 1H), 6.32 (dd, *J* = 10.0, 1.6 Hz, 1H), 6.18 (dt, *J* = 3.3, 1.6 Hz, 1H), 6.10 (d, *J* = 1.9 Hz,

1H), 3.17 (ddd, *J* = 10.5, 8.3, 4.6 Hz, 1H), 3.07–2.99 (m, 1H), 2.77 – 2.69 (m, 2H), 2.40 (s, 3H), 2.16–2.05 (m, 1H), 2.12 (s, 3H), 1.99 (ddd, *J* = 14.1, 11.2, 5.8 Hz, 1H), 1.81–1.67 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.6, 166.9, 147.2, 145.9, 140.0, 130.2, 123.3, 117.5, 111.0, 66.4, 51.5, 36.4, 30.6, 27.8, 19.1, 11.4. FTIR (NaCl, thin film) 2919, 2849, 1669, 1643, 1607, 1512, 1452, 1272, 1176, 1139, 892, 732 cm^{-1}; HRMS (ESI+) calc'd for $C_{16}H_{19}NO_2$ $[M+H]^+$ 258.1489, found 258.1490.

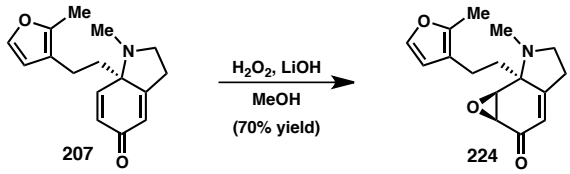
Photochemical [2+2] reaction of dihydroindolone 207.



A solution of dihydroindolone **207** (70 mg, 0.27 mmol) in benzene (36 mL) was divided into six 6 mL portions, which were each placed in 13x100 mm borosilicate test tubes. The reaction tubes were irradiated in a Luzchem photoreactor fitted with λ ≈ 350 nm lamps and a merry-go-round apparatus. After irradiating for 2 hours, the reaction mixtures were combined and concentrated under reduced pressure. The crude residue was purified by flash chromatography (1 to 3% MeOH in CH_2Cl_2) to give a mixture of dihydrofuran **206**, diketone **223**, and small amounts (~10%) of other unidentified products (21 mg total, <30% yield). This mixture of products was further purified by preparative TLC for characterization purposes. Spectral data[17] for dihydrofuran **206**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (d, *J* = 10.5 Hz, 1H), 6.43 (d, *J* = 2.9 Hz, 1H), 6.07 (d, *J* = 10.5 Hz, 1H), 4.84 (d, *J* = 2.9 Hz, 1H), 3.29 (s, 1H), 2.67 (dt, *J* = 8.7, 6.7 Hz, 1H), 2.58 (dt, *J* = 9.0, 6.9 Hz, 1H), 2.47 (s, 3H), 2.36–2.22 (m, 2H), 1.89–1.78 (m, 1H), 1.78–1.63 (m, 3H), 1.27 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.4, 151.5, 147.0, 128.7, 103.5, 89.0, 70.5, 66.9, 61.5, 57.1, 54.3, 35.8, 34.6, 32.2, 28.8, 16.3. Characterization data for diketone **223**: $[\alpha]_D^{25}$ +45.1° (c = 0.45, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (d, *J* = 1.9 Hz, 1H), 6.13 (d, *J* = 1.9 Hz, 1H), 3.16 (ddd, *J* = 9.3, 8.0, 1.2 Hz, 1H), 2.89 (d, *J* = 18.6 Hz, 1H), 2.85 (d, *J* = 5.6 Hz, 1H), 2.78–2.62 (m, 4H), 2.42 (td, *J* = 9.7, 8.2 Hz, 1H), 2.35–2.15 (m, 4H), 2.26 (s, 3H), 2.20 (s, 3H), 1.88 (ddd, *J* = 13.4, 9.8, 8.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 215.5, 209.7, 147.8, 140.2, 117.2, 111.1, 69.2, 62.2, 56.7,

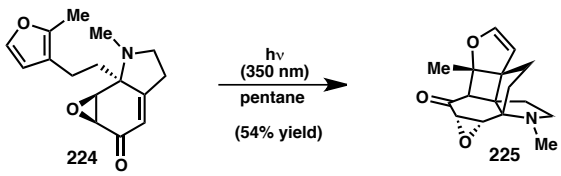
47.3, 41.9, 39.7, 38.9, 34.9, 19.5, 11.4; FTIR (NaCl, thin film) 2919, 2848, 2785, 1745, 1700, 1513, 1452, 1395, 1351, 1252, 1138, 1045, 893, 735 cm^{-1}; HRMS (ESI+) calc'd for $C_{16}H_{21}NO_3$ $[M+H]^+$ 276.1594, found 276.1591.

Preparation of epoxide 224.



To a solution of dienone **207** (213 mg, 0.828 mmol) in MeOH (8 mL) was added LiOH (40.0 mg, 1.66 mmol), followed by aqueous H_2O_2 (101 μL of a 50 wt % H_2O solution, 1.66 mmol). The reaction was allowed to stir at room temperature for 1 hour, then H_2O (8 mL) was added. The mixture was extracted with EtOAc (3 x 20 mL), and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (50 to 75% EtOAc in Hexanes) provided epoxide **224** (158 mg, 70% yield) as a yellow oil. $[\alpha]_D^{25}$ – 235.9° (c = 0.83, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (d, *J* = 1.9 Hz, 1H), 6.13 (d, *J* = 1.8 Hz, 1H), 5.87 (dd, *J* = 3.9, 1.9 Hz, 1H), 3.62 (d, *J* = 4.1 Hz, 1H), 3.42 (dd, *J* = 4.1, 1.8 Hz, 1H), 3.15 (ddd, *J* = 9.4, 7.7, 4.6 Hz, 1H), 2.85 (td, *J* = 9.3, 6.6 Hz, 1H), 2.74–2.66 (m, 2H), 2.56 (s, 3H), 2.20–2.05 (m, 5H), 1.84 (ddd, *J* = 13.8, 11.3, 5.8 Hz, 1H), 1.74 (ddd, *J* = 13.9, 12.0, 5.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.0, 162.6, 147.2, 140.1, 118.5, 117.3, 110.8, 65.4, 53.5, 53.3, 50.9, 35.0, 29.7, 28.5, 19.5, 11.4. FTIR (NaCl, thin film) 2918, 2848, 1676, 1512, 1448, 1273, 1171, 1137, 1055, 893 cm^{-1}; HRMS (ESI+) calc'd for $C_{16}H_{19}NO_3$ $[M+H]^+$ 274.1438, found 274.1438.

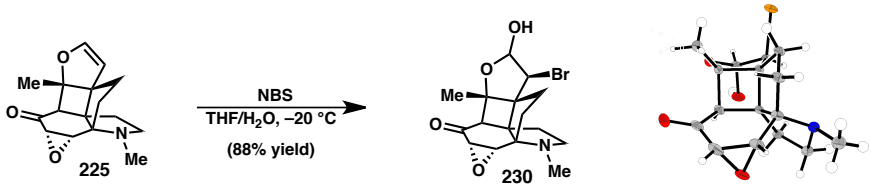
Preparation of dihydrofuran 225.



A solution of enone **224** (38 mg, 0.14 mmol) in a 50:1 mixture of pentane/benzene (24 mL) was divided into four 6 mL portions, which were each placed

in 13x100 mm borosilicate test tubes. The reaction tubes were irradiated in a Luzchem photoreactor fitted with λ ≈ 350 nm lamps and a merry-go-round apparatus. After irradiating for 50 minutes, the reaction mixtures were combined and concentrated under reduced pressure. The crude residue was purified by flash chromatography (50 to 75% EtOAc in Hexanes) to give dihydrofuran **225** (20 mg, 52% yield) as a pale yellow solid. $[\alpha]_D^{25}$ +55.1° (*c* 0.58, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.38 (d, *J* = 2.8 Hz, 1H), 4.65 (d, *J* = 2.8 Hz, 1H), 3.64 (d, *J* = 4.3 Hz, 1H), 3.24 (d, *J* = 4.3 Hz, 1H), 3.18 (s, 1H), 2.97 (td, *J* = 8.6, 5.6 Hz, 1H), 2.77 (ddd, *J* = 8.5, 7.7, 5.6 Hz, 1H), 2.48 (s, 3H), 2.31 (ddd, *J* = 13.1, 7.6, 5.7 Hz, 1H), 2.11 (dd, *J* = 13.8, 7.4 Hz, 1H), 1.95 (ddd, *J* = 13.4, 8.4, 5.6 Hz, 1H), 1.84 (dd, *J* = 13.8, 7.4 Hz, 1H), 1.74 (td, *J* = 13.3, 7.6 Hz, 1H), 1.56 (td, *J* = 13.3, 7.6 Hz, 1H), 1.22 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 204.8, 147.4, 103.0, 89.0, 71.0, 65.5, 62.1, 60.0, 55.8, 55.7, 54.6, 34.6, 32.0, 31.6, 29.8, 16.8. FTIR (NaCl, thin film) 2949, 2930, 2889, 2786, 1699, 1606, 1448, 1187, 1136, 1027, 883, 872 cm^{-1}; HRMS (ESI+) calc'd for $C_{16}H_{19}NO_3$ $[M+H]^+$ 274.1438, found 274.1438.

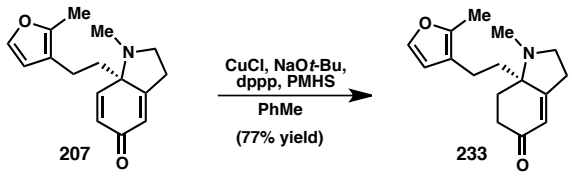
Preparation of bromohydrin 230.



To a solution of dihydrofuran **225** (19 mg, 0.070 mmol) in a 10:1 mixture of THF:H_2O (1.4 mL total) at –20 °C was added *N*-bromosuccinimide (13 mg, 0.075 mmol). The reaction mixture was allowed to stir 30 minutes at –20 °C and then quenched with saturated aqueous $Na_2S_2O_3$ (2 mL). After stirring for 10 minutes and warming to room temperature, the mixture was extracted with EtOAc (3 x 10 mL) and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by flash chromatography (30 to 40% EtOAc in Hexanes) to furnish bromohydrin **230** (23 mg, 88% yield) as a white solid. A small portion of **230** was recrystallized from Et_2O/Hexanes to give crystals suitable for single crystal X-ray diffraction: $[\alpha]_D^{25}$ –7.5° (*c* 1.10, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$; compound exists as a 3:1 mixture of inseparable diastereomers, major diastereomer is designated by *, minor

diastereomer denoted by [§]) δ 5.85 (s, 1H[*]), 5.14 (s, 1H[§]), 4.45 (s, 1H[§]), 4.44 (s, 1H[*]), 3.65 (d, *J* = 4.5 Hz, 1H[§]), 3.64 (d, *J* = 4.4 Hz, 1H[*]), 3.31 (s, 1H[*]), 3.23 (d, *J* = 4.4 Hz, 1H[§]), 3.21 (d, *J* = 4.3 Hz, 1H[*]), 3.03 – 2.98 (t, *J* = 6.9 Hz, 2H[§]), 2.97 – 2.91 (m, 1H[*]), 2.97 – 2.91 (m, 2H[§]), 2.54 (dt, *J* = 14.6, 7.4 Hz, 1H[*]), 2.49 (s, 3H[*]), 2.48 (s, 3H[§]), 2.20 – 2.06 (m, 1H[*], 2H[§]), 2.06 – 1.98 (m, 2H[*], 2H[§]), 1.93 (ddd, *J* = 14.3, 7.6, 5.4 Hz, 1H[*]), 1.44 (ddd, *J* = 14.0, 12.8, 7.5 Hz, 1H[*]), 1.39 (ddd, *J* = 14.1, 12.9, 7.4 Hz, 1H[§]), 1.29 (s, 3H[*], 3H[§]), 0.88 (m, 1H[§]); ^{13}C NMR (126 MHz, $CDCl_3$) δ 204.8[*], 203.9[§], 106.5[*], 95.6[§], 89.2[*], 83.9[§], 73.54[*], 73.48[§], 64.4[*], 63.5[*], 63.0[§], 58.6[*], 58.1[§], 57.6[§], 57.0[*], 56.3[*], 56.1[§], 55.1[§], 54.58[§], 54.57[*], 54.51[*], 54.3[§], 34.5[*], 34.3[§], 32.8[*], 32.0[*], 31.8[§], 30.02[§], 29.96[*], 29.87[§], 18.8[*], 18.2[§]. FTIR (NaCl, thin film) 3413, 2937, 2854, 1701, 1449, 1379, 1255, 1215, 1177, 1021, 930, 877, 737 cm^{-1}; HRMS (ESI+) calc'd for $C_{16}H_{20}NO_4Br$ $[M+H]^+$ 370.0648, found 370.0641.

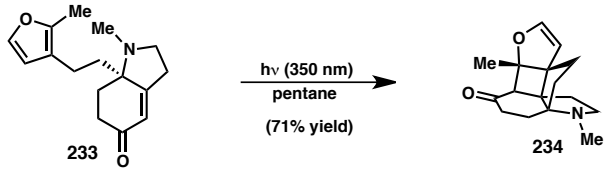
Preparation of enone 233.



In a glove box, a round bottom flask was charged with CuCl (8.6 mg, 0.087 mmol), NaO*t*-Bu (8.4 mg, 0.087 mmol), dppp (36 mg, 0.087 mmol), and degassed PhMe (5.7 mL), and the mixture was stirred for 20 minutes. The reaction was brought out onto the benchtop, placed under an atmosphere of N_2, and polymethylhydrosiloxane (58 μL, 0.96 mmol) was added, followed by a solution of dihydroindolone **207** (225 mg, 0.87 mmol) in degassed PhMe (3 mL). The reaction was allowed to stir 2 hours, then quenched by the addition of aqueous 1 N NaOH (9 mL) and stirred vigorously for 20 minutes. The mixture was extracted with EtOAc (2 x 30 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by flash chromatography (0 to 3% MeOH in CH_2Cl_2) to give enone **233** (170 mg, 75% yield) as a yellow oil. $[\alpha]_D^{25}$ –115.9° (*c* 0.28, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (d, *J* = 1.8 Hz, 1H), 6.15 (d, *J* = 1.8 Hz, 1H), 5.87 – 5.83 (m, *J* = 1.5 Hz, 1H), 3.02 – 2.92 (m, 2H), 2.73 (dddd, *J* = 17.7, 8.1, 5.9, 2.3 Hz, 1H), 2.65 (dddd, *J* = 17.8, 7.4, 5.9, 1.4 Hz, 1H), 2.49 – 2.41 (m, 3H), 2.46 (s, 3H), 2.41 – 2.30 (m, 1H), 2.25

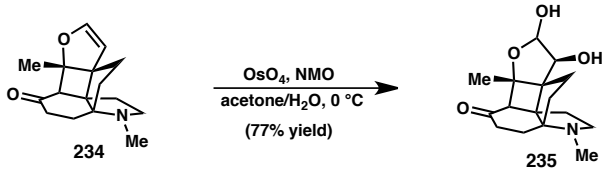
(ddd, *J* = 12.8, 5.0, 2.4 Hz, 1H), 2.19 (s, 3H), 1.87 (td, *J* = 13.0, 7.0, 1H), 1.82 (ddd, *J* = 14.2, 12.4, 4.8 Hz, 1H), 1.68 (ddd, *J* = 14.3, 12.7, 5.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.7, 172.7, 147.0, 140.0, 121.5, 118.4, 111.0, 63.2, 51.7, 35.0, 33.6, 33.3, 31.6, 30.3, 21.4, 11.5; FTIR (NaCl, thin film) 2923, 2784, 1669, 1448, 1270, 1198, 1137, 892, 729 cm^{-1}; HRMS (ESI+) calc'd for $C_{16}H_{21}NO_2$ $[M+H]^+$ 260.1645, found 260.1645.

Preparation of dihydrofuran 234.



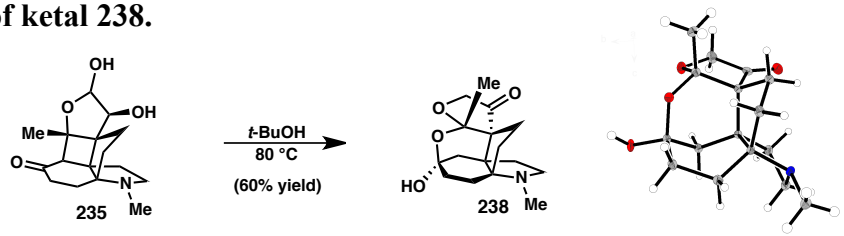
A solution of enone **233** (170 mg, 0.66 mmol) in a 50:1 mixture of pentane/benzene (65 mL) was divided into ten 6.5 mL portions, which were each placed in 13x100 mm borosilicate test tubes. The reaction tubes were irradiated in a Luzchem photoreactor fitted with λ ≈ 350 nm lamps and a merry-go-round apparatus. After irradiating for 6 hours, the reaction mixtures were combined and concentrated under reduced pressure. The crude residue was purified by flash chromatography (2 to 8% MeOH in CH_2Cl_2) to give dihydrofuran **234** (120 mg, 71% yield) as a pale yellow solid. $[\alpha]_D^{25}$ +207.6° (*c* 0.37, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.36 (d, *J* = 2.8 Hz, 1H), 4.74 (d, *J* = 2.8 Hz, 1H), 3.10 (s, 1H), 2.76 – 2.65 (m, 2H), 2.52 – 2.43 (m, 1H), 2.35 – 2.23 (m, 2H), 2.28 (s, 3H), 1.97 – 1.84 (m, 3H), 1.83 – 1.72 (m, 3H), 1.64 (ddd, *J* = 13.9, 8.2, 6.7 Hz, 1H), 1.24 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 209.9, 146.6, 104.1, 88.5, 71.1, 65.3, 62.3, 60.2, 53.0, 37.0, 34.5, 31.5, 30.7, 29.6, 24.1, 16.9; FTIR (NaCl, thin film) 2925, 2864, 2783, 1696, 1600, 1457, 1379, 1169, 1139, 1031, 879, 755 cm^{-1}; HRMS (ESI+) calc'd for $C_{16}H_{21}NO_2$ $[M+H]^+$ 260.1645, found 260.1644.

Preparation of diol 235.



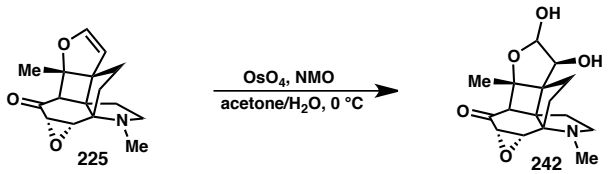
To a solution of dihydrofuran **234** (93 mg, 0.36 mmol) in acetone (6.4 mL) at 0 °C was added OsO_4 (23 μL of a 4 wt % solution in H_2O, 3.6 μmol), followed by a solution of *N*-methylmorpholine-*N*-oxide (46 mg, 0.39 mmol) in H_2O (0.6 mL). The resulting solution was allowed to stir 45 minutes at 0 °C. The reaction was quenched by the addition of saturated aqueous $Na_2S_2O_3$ (6 mL), and the resulting mixture was stirred at 0 °C for 20 minutes. The biphasic mixture was warmed to room temperature and extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by flash chromatography (5 to 20% MeOH in CH_2Cl_2) to provide diol **235** (81 mg, 77% yield) as an off-white foam. $[\alpha]_D^{25}$ +116.4° (*c* 0.56, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$; compound exists as a 2:1 mixture of inseparable diastereomers[4], major diastereomer is designated by *, minor diastereomer denoted by §) δ 5.50 (s, 1H§), 5.37 (d, *J* = 2.9 Hz, 1H*), 4.23 (s, 1H§), 3.92 (d, *J* = 2.8 Hz, 1H*), 3.30 (s, 1H§), 2.99–2.82 (m, 1H*, 1H§), 2.85 (s, 1H*), 2.79 (td, *J* = 9.3, 6.0 Hz, 1H*), 2.76–2.69 (m, 1H§), 2.60–2.54 (m, 1H§), 2.54–2.45 (m, 1H*, 1H§), 2.37–2.20 (m, 2H*, 1H§), 2.32 (s, 3H§), 2.31 (s, 3H*), 2.18 (ddd, *J* = 14.1, 8.2, 6.0 Hz, 1H*), 1.97–1.82 (m, 3H*, 3H§), 1.82–1.71 (m, 2H*, 2H§), 1.71–1.59 (m, 1H*, 1H§), 1.20 (s, 3H*, 3H§); ^{13}C NMR (126 MHz, $CDCl_3$) δ 210.6§, 209.3*, 106.1§, 97.7*, 88.3§, 84.3*, 79.4§, 74.0*, 73.3§, 72.8*, 64.6§, 62.5*, 61.7§, 59.8*, 54.9§, 54.1*, 53.0§, 52.9*, 36.31§, 36.27*, 34.7§, 34.6*, 31.4§, 30.0*, 29.7§, 29.1*, 29.0§, 26.1*, 22.2*, 21.8§, 18.8§, 18.6*; FTIR (NaCl, thin film) 3369, 2935, 2864, 2788, 1691, 1448, 1183, 1146, 1125, 1049, 1022, 979, 914, 875, 754 cm^{-1}; HRMS (ESI+) calc'd for $C_{16}H_{23}NO_4$ $[M+H]^+$ 294.1700, found 294.7001.

Preparation of ketal 238.



A 20-mL vial was charged with diol **235** (30 mg, 0.10 mmol) and *t*-BuOH (3 mL), sealed, and heated to 80 °C for 5 days. The reaction mixture was cooled to room temperature, concentrated under reduced pressure, and purified by flash chromatography (2 to 8% MeOH in CH_2Cl_2) to give ketal **238** (18 mg, 60% yield) as a pale yellow solid. $[\alpha]_D^{25}$ +47.9° (*c* 0.47, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.12 (d, *J* = 17.7 Hz, 1H), 3.90 (d, *J* = 17.7 Hz, 1H), 2.97 (s, 1H), 2.88 (q, *J* = 8.6 Hz, 1H), 2.67 (td, *J* = 9.5, 2.3 Hz, 1H), 2.28 – 2.20 (m, 1H), 2.25 (s, 3H), 2.18 (dd, *J* = 13.4, 1.7 Hz, 1H), 2.01–1.94 (m, 1H), 1.93 (d, *J* = 13.4 Hz, 1H), 1.88–1.71 (m, 3H), 1.69–1.61 (m, 2H), 1.59–1.49 (m, 1H), 1.42–1.36 (m, 1H), 1.35 (s, 3H), 1.04 (ddd, *J* = 12.7, 7.1, 2.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 214.1, 109.8, 97.3, 73.1, 69.2, 60.4, 55.4, 51.2, 36.2, 35.2, 34.1, 31.3, 29.4, 26.6, 24.3, 24.2; FTIR (NaCl, thin film) 3066, 2966, 2938, 2804, 1744, 1452, 1353, 1313, 1240, 1185, 1129, 1074, 1055, 1002, 900, 876, 859 cm^{-1}; HRMS (ESI+) calc'd for $C_{16}H_{23}NO_4$ $[M+H]^+$ 294.1700, found 294.1705.

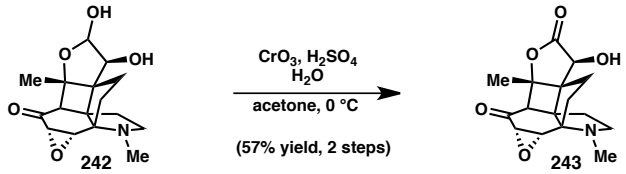
Preparation of diol 242.



To a solution of dihydrofuran **225** (400 mg, 1.46 mmol) in acetone (27 mL) at 0 °C was added OsO_4 (150 µL of a 2.5 wt % solution in *t*-BuOH, 14.6 µmol), followed by a solution of NMO (175 mg, 1.49 mmol) in H_2O (2 mL). The reaction was allowed to stir for 1 hour at 0 °C, quenched by the addition of saturated aqueous $Na_2S_2O_3$ (15 mL), and stirred at 0 °C for an additional 20 minutes. The mixture was warmed to room temperature and extracted with EtOAc (3 x 30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a pale yellow oil. The crude product was used in the following step without further purification.

A small sample was purified by flash chromatography (4 to 10% MeOH in CH_2Cl_2) to provide diol **242** as a white foam: $[\alpha]_D^{25}$ +21.9° (*c* 1.20, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, compound exists as a 1.5:1 mixture of inseparable diastereomers) δ 5.47 (s, 1H), 5.40 (d, *J* = 3.0 Hz, 1H), 4.20 (s, 1H), 3.89 (d, *J* = 3.0 Hz, 1H), 3.66 (d, *J* = 4.4 Hz, 1H), 3.66 (d, *J* = 4.3 Hz, 1H), 3.28 (s, 1H), 3.23 (d, *J* = 4.4 Hz, 1H), 3.20 (d, *J* = 4.3 Hz, 1H), 3.06–2.91 (m, 4H), 2.86 (s, 1H), 2.61–2.46 (m, 1H), 2.50 (s, 3H), 2.49 (s, 3H), 2.19–2.02 (m, 5H), 2.02–1.79 (m, 4H), 1.55–1.36 (m, 2H), 1.22 (s, 3H), 1.20 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.2, 204.4, 105.9, 97.8, 88.7, 84.8, 79.3, 74.1, 73.3, 73.0, 64.7, 62.4, 58.5, 58.4, 57.1, 55.1, 54.8, 54.7, 54.52, 54.47, 54.4, 54.0, 34.9, 34.7, 31.2, 30.7, 30.5, 30.3, 26.8, 19.1, 18.8; FTIR (NaCl, thin film) 3369, 2935, 2864, 2788, 1691, 1448, 1183, 1146, 1125, 1049, 1022, 979, 914, 875, 754 cm^{-1}; HRMS (ESI+) calc'd for $C_{16}H_{21}NO_5$ $[M+H]^+$ 308.1492, found 308.1494.

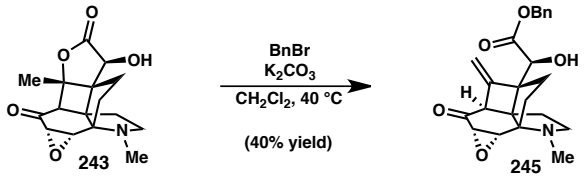
Preparation of lactone 243.



To a solution of diol **242** (1.46 mmol) in acetone (30 mL) at 0 °C was added a solution of chromic acid (3.1 M based on CrO_3, 1.9 mL) dropwise by syringe over 1 minute. The reaction was allowed to stir at 0 °C for an additional 7 minutes, then quenched by the sequential addition of *i*-PrOH (0.5 mL) and saturated aqueous $NaHCO_3$ (15 mL). The mixture was warmed to room temperature and stirred vigorously for 5 minutes, then diluted and extracted with EtOAc (4 x 20 mL). The combined organic layers were washed with brine (30 mL), dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by flash chromatography (2 to 4% MeOH in CH_2Cl_2) to deliver lactone **243** (253 mg, 57% yield, 2 steps) as a white foam: $[\alpha]_D^{25}$ –42.2° (*c* 0.60, $CHCl_3$); 1H NMR (500 MHz, $CDCl_3$) δ 5.26 (s, 1H), 4.06 (s, 1H), 3.73 (d, J = 4.6 Hz, 1H), 3.36 (ddd, J = 9.6, 7.2, 5.1 Hz, 1H), 3.32 (d, J = 4.6 Hz, 1H), 3.02 (ddd, J = 9.6, 8.6, 7.4 Hz, 1H), 2.93 (s, 1H), 2.50 (s, 3H), 2.31 (ddd, J = 14.7, 12.9, 8.1 Hz, 1H), 2.16 (dd, J = 14.3, 8.0 Hz, 1H), 2.13–2.05 (m, 2H), 1.86 (dd, J = 14.7, 7.6 Hz, 1H), 1.47–1.36 (m,

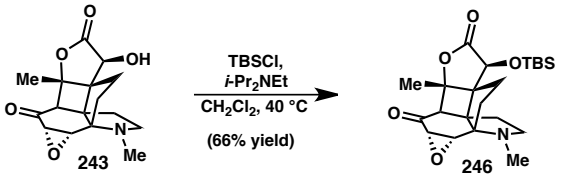
1H), 1.40 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.3, 176.0, 90.4, 74.0, 71.6, 59.1, 57.9, 56.7, 54.9, 54.4, 34.5, 30.6, 30.1, 25.5, 18.0; FTIR (NaCl, thin film) 3421, 2944, 2860, 1773, 1707, 1449, 1384, 1256, 1171, 1081, 953, 873, 737 cm^{-1}; HRMS (ESI+) calc'd for $C_{16}H_{19}NO_5$ $[M+H]^+$ 306.1336, found 306.1341.

Preparation of cyclobutane 245.



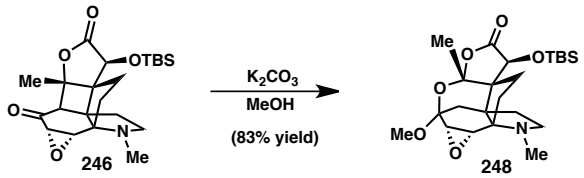
To a solution of lactone **243** (10 mg, 0.033 mmol) in CH_2Cl_2 (0.7 mL) was added BnBr (8 μL, 0.07 mmol), followed by Cs_2CO_3 (22 mg, 0.07 mmol). The reaction was heated to 40 °C and allowed to stir 5 hours. The reaction was cooled to room temperature, then quenched with saturated aqueous NH_4Cl (1 mL). The mixture was extracted with EtOAc (3 x 2 mL), and the combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by preparative TLC (80% EtOAc in Hexanes) to generate cyclobutane **245** (5.2 mg, 40% yield) as a white solid: $[\alpha]_D^{25}$ –15.8° (*c* 0.26, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41–7.32 (m, 5H), 5.23 (dd, *J* = 3.0, 1.1 Hz, 1H), 5.20 (m, 2H), 4.81 (dd, *J* = 3.5, 1.1 Hz, 1H), 4.34 (s, 1H), 3.65 (d, *J* = 4.4 Hz, 1H), 3.36 (t, *J* = 3.2 Hz, 1H), 3.22 (dd, *J* = 4.3, 0.5 Hz, 1H), 3.04 (td, *J* = 8.7, 3.9 Hz, 1H), 2.89 (td, *J* = 9.1, 8.7, 6.1 Hz, 1H), 2.51–2.43 (m, 1H), 2.48 (s, 3H), 2.09 (td, *J* = 12.4, 7.0 Hz, 1H), 2.01–1.90 (m, 2H), 1.58 (dd, *J* = 12.6, 6.9 Hz, 1H), 1.47 (ddd, *J* = 13.4, 12.3, 6.9 Hz, 1H), 1.25 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 204.3, 172.9, 145.0, 134.6, 128.9, 128.8, 128.7, 111.3, 72.0, 71.6, 67.6, 63.1, 58.5, 58.0, 54.4, 54.3, 51.2, 34.3, 30.8, 30.3, 29.6; FTIR (NaCl, thin film) 3493, 2924, 2853, 1735, 1706, 1455, 1262, 1216, 1195, 1105, 1071, 909, 879, 754 cm^{-1}; HRMS (ESI+) calc'd for $C_{23}H_{25}NO_5$ $[M+H]^+$ 396.1805, found 396.1809.

Preparation of silyl ether 246.



To a solution of **243** (70 mg, 0.23 mmol) in CH_2Cl_2 (1.2 mL) was added TBSCl (42 mg, 0.28 mmol), followed by *i*-Pr_2NEt (80 μL, 0.46 mmol). The reaction was heated to 40 °C and stirred for 4 hours, then cooled to room temperature and quenched with saturated aqueous $NaHCO_3$ (2 mL). The resulting mixture was extracted with EtOAc (3 x 5 mL), and the combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure. The crude residue was purified by flash chromatography (25 to 33% EtOAc in Hexanes) to give silyl ether **246** (63 mg, 66% yield) as a colorless oil: $[\alpha]_D^{25}$ –28.1° (*c* 0.45, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.02 (s, 1H), 3.68 (d, *J* = 4.5 Hz, 1H), 3.31 (d, *J* = 4.6 Hz, 1H), 2.99 (td, *J* = 9.1, 5.0 Hz, 1H), 2.95–2.88 (m, 1H), 2.90 (s, 1H), 2.47 (s, 3H), 2.18–2.05 (m, 2H), 2.04–1.87 (m, 2H), 1.83 (ddd, *J* = 14.4, 7.4, 1.0 Hz, 1H), 1.40 (s, 3H), 1.32 (ddd, *J* = 14.0, 12.8, 7.4 Hz, 1H), 0.86 (s, 9H), 0.15 (d, *J* = 5.2 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 204.2, 174.4, 90.2, 73.2, 73.1, 59.7, 59.0, 56.2, 55.8, 54.5, 54.1, 34.4, 30.4, 29.9, 26.9, 25.6, 18.2, 17.8, -4.7, -5.3; FTIR (NaCl, thin film) 2955, 2930, 2857, 1781, 1709, 1472, 1383, 1255, 1171, 1090, 1044, 946, 840, 781 cm^{-1}; HRMS (ESI+) calc'd for $C_{22}H_{33}NO_5Si$ $[M+H]^+$ 420.2201, found 420.2203.

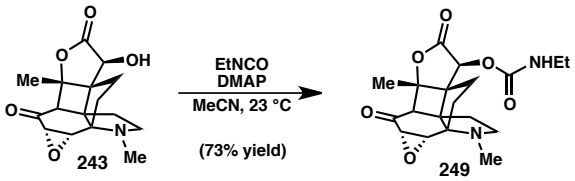
Preparation of ketal 248.



To a solution of silyl ether **246** (17 mg, 0.040 mmol) in MeOH (1.3 mL) at 0 °C was added K_2CO_3 (11 mg, 0.079 mmol) in one portion. The solution was warmed to room temperature and stirred for 2 hours. The reaction mixture was quenched with saturated aqueous NH_4Cl (1 mL) and extracted with EtOAc (3 x 2 mL). The combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by flash chromatography (25 to 40% EtOAc in Hexanes) to give ketal **248** (15

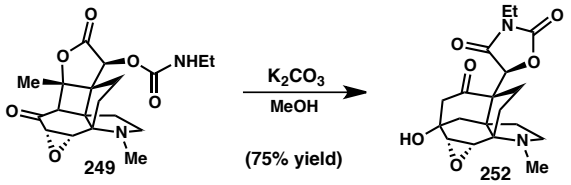
mg, 83% yield) as a colorless oil: $[\alpha]_D^{25}$ –52.3° (*c* 0.35, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.07 (s, 1H), 3.42 (s, 3H), 3.30 (dd, *J* = 4.8, 1.5 Hz, 1H), 3.24 (d, *J* = 4.8 Hz, 1H), 2.91 (dd, *J* = 8.8, 6.3 Hz, 1H), 2.81 (ddd, *J* = 11.7, 8.8, 4.2 Hz, 1H), 2.59 (s, 3H), 2.07 (d, *J* = 14.0 Hz, 1H), 2.01–1.92 (m, 2H), 1.78 (td, *J* = 11.5, 6.5 Hz, 1H), 1.68 (s, 3H), 1.65 (dd, *J* = 14.0, 1.6 Hz, 1H), 1.62–1.54 (m, 1H), 1.48–1.31 (m, 2H), 0.88 (s, 9H), 0.16 (d, *J* = 2.0 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.8, 112.4, 99.7, 75.2, 71.3, 60.2, 56.2, 55.0, 53.9, 53.7, 50.0, 36.0, 35.6, 33.4, 27.2, 26.3, 25.6, 25.5, 18.1, -4.6, -5.2; FTIR (NaCl, thin film) 2929, 2855, 1783, 1469, 1379, 1274, 1257, 1186, 1123, 1040, 1024, 994, 928, 843, 781 cm^{-1}; HRMS (ESI+) calc'd for $C_{23}H_{37}NO_6Si$ $[M+H]^+$ 452.2463, found 452.2471.

Preparation of carbamate 249.



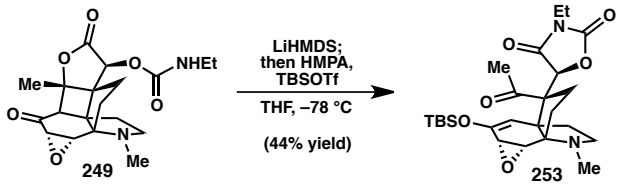
To a solution of lactone **243** (350 mg, 1.15 mmol) in MeCN (6 mL) was sequentially added ethyl isocyanate (200 μL, 2.52 mmol) and DMAP (140 mg, 1.15 mmol). The reaction was allowed to stir for 4 hours, then concentrated under reduced pressure and loaded directly onto a silica gel column. Flash chromatography (80 to 100% EtOAc in Hexanes) afforded carbamate **249** (314 mg, 73% yield) as a white foam: $[\alpha]_D^{25}$ –46.0° (*c* 0.70, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.22 (s, 1H), 4.80 (t, *J* = 5.9 Hz, 1H), 3.67 (d, *J* = 4.4 Hz, 1H), 3.32 (d, *J* = 4.4 Hz, 1H), 3.28–3.17 (m, 2H), 3.05–2.96 (m, 2H), 2.93 (s, 1H), 2.46 (s, 3H), 2.23–2.08 (m, 3H), 1.89 (ddd, *J* = 14.0, 12.8, 7.6 Hz, 1H), 1.77 (dd, *J* = 14.0, 7.2 Hz, 1H), 1.46 – 1.33 (m, 1H), 1.40 (s, 3H), 1.14 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.6, 172.4, 154.5, 89.8, 72.6, 71.9, 59.1, 58.1, 57.1, 55.8, 54.1, 53.8, 36.3, 34.3, 30.5, 30.2, 26.1, 17.5, 15.0; FTIR (NaCl, thin film) 3370, 2939, 1777, 1730, 1708, 1525, 1450, 1382, 1239, 1173, 1138, 1085, 1027, 959, 872, 732 cm^{-1}; HRMS (ESI+) calc'd for $C_{19}H_{24}N_2O_6$ $[M+H]^+$ 377.1707, found 377.1711.

Preparation of alcohol 252.



To a solution of carbamate **249** (4.0 mg, 0.011 mmol) in MeOH (0.8 mL) was added K_2CO_3 (3 mg, 0.02 mmol) in one portion. The reaction was allowed to stir at room temperature for 3 hours, then quenched with saturated aqueous NH_4Cl (1 mL). The mixture was diluted and extracted with EtOAc (3 x 2 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash chromatography (1 to 3% MeOH in CH_2Cl_2) to deliver alcohol **252** (3.0 mg, 75% yield) as a white solid: $[\alpha]_D^{25}$ +139.2° (*c* 0.75, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.19–4.97 (m, 1H), 4.57 (s, 1H), 3.98 (d, *J* = 4.5 Hz, 1H), 3.68–3.52 (m, 2H), 3.39 (ddd, *J* = 10.1, 8.4, 4.7 Hz, 1H), 3.11–3.04 (m, 1H), 2.93 (d, *J* = 19.4 Hz, 1H), 2.80–2.68 (m, 2H), 2.67–2.58 (m, 1H), 2.47 (d, *J* = 19.4 Hz, 1H), 2.40 (s, 3H), 2.31 (ddd, *J* = 15.1, 9.7, 2.3 Hz, 1H), 2.17–2.03 (m, 2H), 1.80 (ddd, *J* = 13.7, 8.4, 6.6 Hz, 1H), 1.65 (dt, *J* = 15.7, 9.8 Hz, 1H), 1.29 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (126 MHz, cdcl$_3$) δ 207.1, 172.5, 154.9, 80.8, 75.7, 72.3, 67.8, 58.2, 52.7, 52.7, 49.1, 44.5, 39.4, 37.0, 35.3, 33.0, 30.1, 28.1, 12.2; FTIR (NaCl, thin film) 2947, 1810, 1733, 1697, 1449, 1420, 1350, 1220, 1055, 1017, 958, 765, 734 cm^{-1}; HRMS (ESI+) calc'd for $C_{19}H_{24}N_2O_6$ $[M+H]^+$ 377.1707, found 377.1718.

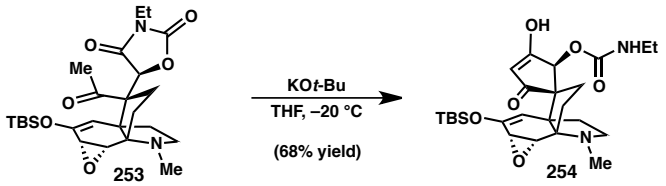
Preparation of silyl enol ether 253.



To a solution of carbamate **249** (47.0 mg, 0.125 mmol) in THF (1.6 mL) at –78 °C was added LiHMDS (137 µL, 0.137 mmol) dropwise via syringe. The reaction was stirred at –78 °C for 20 minutes, then HMPA (239 µL, 1.37 mmol) and TBSOTf (34 µL, 0.15 mmol) were sequentially added via syringe. The resulting mixture was stirred for an

additional 20 minutes at –78 °C before quenching with 2,6-lutidine (14 μL, 0.125 mmol) followed by aqueous buffer solution (pH= 7, 2 mL). The mixture was allowed to warm to room temperature, diluted with additional buffer solution (5 mL), then extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by flash chromatography on Florisil (40 to 60% EtOAc in Hexanes) to afford silyl enol ether **253** (27 mg, 44% yield) as a white foam: $[\alpha]_D^{25}$ –111.3° (*c* 1.23, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.03 (d, *J* = 2.1 Hz, 1H), 4.75 (s, 1H), 3.68–3.53 (m, 2H), 3.42 (d, *J* = 4.2 Hz, 1H), 3.10 (dd, *J* = 4.2, 2.1 Hz, 1H), 2.95 (ddd, *J* = 9.5, 8.6, 5.8 Hz, 1H), 2.79 (ddd, *J* = 8.7, 6.9, 2.0 Hz, 1H), 2.65 (s, 3H), 2.42–2.21 (m, 3H), 2.14–2.05 (m, 1H), 2.10 (s, 3H), 2.00 (ddd, *J* = 13.9, 12.2, 7.9 Hz, 1H), 1.89 (ddd, *J* = 12.8, 5.8, 2.0 Hz, 1H), 1.31 (t, *J* = 7.2 Hz, 3H), 0.91 (s, 9H), 0.22–0.07 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 207.5, 172.1, 155.6, 146.2, 111.4, 83.1, 71.8, 70.9, 60.1, 56.3, 52.7, 50.0, 36.6, 35.6, 35.1, 34.3, 33.0, 29.6, 25.6, 18.0, 12.2, -4.60, -4.62; FTIR (NaCl, thin film) 2956, 2931, 2858, 1813, 1739, 1699, 1668, 1449, 1417, 1381, 1355, 1255, 1221, 1117, 1008, 938, 900, 868, 838, 738 cm^{-1}; HRMS (ESI+) calc'd for $C_{25}H_{38}N_2O_6Si$ $[M+H]^+$ 491.2572, found 491.2579.

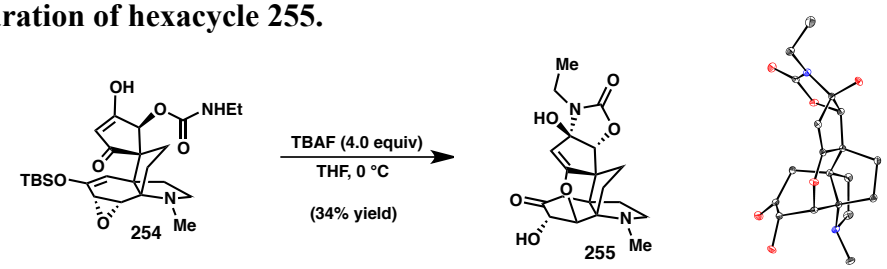
Preparation of cyclopentenone 254.



To a solution of silyl enol ether **253** (44 mg, 0.090 mmol) in THF (3 mL) at –20 °C was added a solution of KO*t*-Bu (99 μL, 1.0 M in THF, 0.099 mmol) dropwise by syringe. The reaction was allowed to stir at –20 °C for 20 minutes, then quenched by the addition of saturated aqueous $NaHCO_3$ (10 mL). The resulting mixture was warmed to room temperature and extracted with a 4:1 mixture of EtOAc/CH_2Cl_2 (9 x 15 mL). The combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by flash chromatography (50 to 60% EtOAc in Hexanes) to furnish cyclopentenone **254** (30 mg, 68% yield) as a white solid: $[\alpha]_D^{25}$ +6.4° (*c* 0.76, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.31 (s, 1H), 5.12 (s, 1H), 4.86 (s, 1H), 4.82 (t, *J* = 5.8 Hz,

1H), 4.75 (d, *J* = 3.2 Hz, 1H), 4.70 (s, 1H), 3.76 (d, *J* = 3.2 Hz, 1H), 3.34–3.19 (m, 3H), 2.64–2.48 (m, 2H), 2.35 (s, 3H), 2.26–2.14 (m, 1H), 2.08 (td, *J* = 13.5, 12.9, 3.5 Hz, 1H), 1.91 (ddd, *J* = 13.4, 9.9, 3.4 Hz, 1H), 1.68 (ddd, *J* = 13.7, 10.0, 6.5 Hz, 1H), 1.61–1.51 (m, 1H), 1.17 (t, *J* = 7.2 Hz, 3H), 0.92 (s, 9H), 0.12 (d, *J* = 13.3 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.2, 191.6, 155.7, 150.0, 109.2, 106.8, 86.1, 75.5, 70.1, 69.9, 59.7, 53.0, 53.0, 37.1, 36.3, 30.9, 30.2, 25.7, 24.0, 18.1, 15.2, -4.20, -4.32; FTIR (NaCl, thin film) 3305, 2930, 2858, 1728, 1698, 1597, 1537, 1463, 1382, 1251, 1211, 1168, 1137, 1086, 1032, 951, 856, 838, 782, 733 cm^{-1}; HRMS (ESI+) calc'd for $C_{25}H_{38}N_2O_6Si$ $[M+H]^+$ 491.2572, found 491.2575.

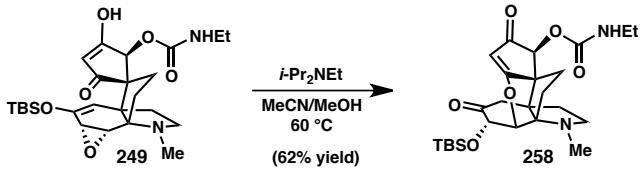
Preparation of hexacycle 255.



To a solution of cyclopentenone **254** (12.6 mg, 0.026 mmol) in THF (2.5 mL) at 0 °C was added TBAF (1.0 M in THF, 103 μL, 0.10 mmol) dropwise by syringe. The reaction was stirred for 30 minutes, then quenched by the addition of saturated aqueous Na_2SO_4 (2 mL). The resulting mixture was extracted with EtOAc (3 x 5 mL), and the combined organic layers were washed with saturated aqueous Na_2SO_4 (4 mL), dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by flash chromatography (50 to 80% EtOAc in Hexanes) to deliver hexacycle **255** (3.3 mg, 34% yield) as a white solid. A portion of this material was recrystallized from $CHCl_3$ to give crystals suitable for single crystal X-ray diffraction: $[\alpha]_D^{25}$ +87.1° (*c* 0.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.16 (d, *J* = 0.7 Hz, 1H), 4.55 (s, 1H), 4.48 (d, *J* = 0.7 Hz, 1H), 3.76 (s, 1H), 3.41 (dq, *J* = 14.4, 7.2 Hz, 1H), 3.27 (dq, *J* = 14.5, 7.3 Hz, 1H), 3.16 (dt, *J* = 9.9, 8.2 Hz, 1H), 2.93 (s, 1H), 2.60 (ddd, *J* = 11.3, 10.0, 3.0 Hz, 1H), 2.40–2.30 (m, 2H), 2.30–3.21 (m, 1H), 2.22 (s, 3H), 2.13–1.99 (m, 2H), 1.94–1.79 (m, 2H), 1.61 (ddd, *J* = 13.9, 10.1, 6.2 Hz, 1H), 1.24 (t, *J* = 7.2 Hz, 7H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 207.8, 162.8, 155.4, 100.73, 96.5, 89.3, 86.2, 75.2, 69.4, 59.8, 55.8, 51.7, 43.5, 36.1, 35.9, 32.9, 32.7, 22.3, 14.8; FTIR (NaCl, thin film) 3332, 2924, 2853, 1720, 1656, 1461, 1376, 1251, 1200,

1091, 1052, 959, 923, 820, 761, 733 cm^{-1}; HRMS (ESI+) calc'd for $C_{19}H_{24}N_2O_6$ $[M+H]^+$ 377.1707, found 377.1716.

Preparation of pentacycle 258.



To a solution of cyclopentenone **249** (21.2 mg, 0.043 mmol) in MeCN/MeOH (4:1, 2 mL total) was added *i*-Pr_2NEt (30 μL, 0.173 mmol). The reaction was heated to 60 °C and allowed to stir for 64 hours at that temperature, then cooled to room temperature and concentrated under reduced pressure. Purification by flash chromatography (40 to 60% EtOAc in Hexanes) afforded pentacycle **258** (13.1 mg, 62% yield) as a white foam: $[\alpha]_D^{25}$ +25.9° (*c* 0.66, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.53 (s, 1H), 5.16 (s, 1H), 4.98 (t, *J* = 5.7 Hz, 1H), 4.75 (s, 1H), 3.82 (s, 1H), 3.22 (m, 2H), 3.14 (ddd, *J* = 9.7, 8.5, 7.4 Hz, 1H), 2.62–2.49 (m, 2H), 2.39 (d, *J* = 15.9 Hz, 1H), 2.22 (s, 3H), 2.12 (td, *J* = 12.1, 7.1 Hz, 1H), 2.05 (d, *J* = 16.0 Hz, 1H), 2.00 (ddd, *J* = 13.6, 10.1, 3.6 Hz, 1H), 1.92 (ddd, *J* = 13.8, 12.3, 3.6 Hz, 1H), 1.63 (ddd, *J* = 14.0, 10.1, 6.4 Hz, 1H), 1.49 (ddd, *J* = 13.3, 8.5, 3.2 Hz, 1H), 1.15 (t, *J* = 7.3 Hz, 3H), 0.91 (s, 10H), 0.13 (d, *J* = 27.9 Hz, 6H); ^{13}C NMR (126 MHz, $cdcl_3$) δ 204.3, 199.3, 190.8, 155.3, 107.2, 95.8, 75.6, 74.9, 69.2, 58.4, 53.8, 51.5, 44.6, 36.2, 35.9, 32.9, 32.0, 25.8, 22.1, 18.4, 15.1, -4.37, -5.56; FTIR (NaCl, thin film) 3342, 2953, 2930, 2855, 1720, 1601, 1535, 1472, 1462, 1380, 1248, 1172, 1144, 1032, 926, 842, 781, 733 cm^{-1}; HRMS (ESI+) calc'd for $C_{25}H_{38}N_2O_6Si$ $[M+H]^+$ 491.2572, found 491.2574.

4.7. Notes and References

(1) Liu, G.; Cogan, D. A.; Owens, T. D.; Tang, T. P.; Ellman, J. A. *J. Org. Chem.* **1999**, *64*, 1278–1284.

(2) Chuang, K. V.; Navarro, R.; Reisman, S. E. *Chem. Sci.* **2011**, *2*, 1086–1089.

(3) Chuang, K. V.; Navarro, R.; Reisman, S. E. *Angew. Chem. Int. Ed.* **2011**, *50*, 9447–9451.

(4) For recent reviews, see: (a) Zeng, X. *Chem. Rev.* **2013**, *113*, 6864–6900; (b) Severin, R.; Doye, S. *Chem. Soc. Rev.* **2007**, *36*, 1407.

(5) Enol ether **215** was isolated in 54% yield as a difficult to separate 9:1 mixture with an unidentified side product. Analytically pure material was obtained by multiple purifications. See: Navarro, R.; Reisman, S.E. *Org. Lett.* **2012**, *14*, 4354–4357.

(6) For examples of intramolecular [2+2] photocycloadditions between furan and enone systems, see: (a) Fontana, G.; Savona, G.; Vivona, N.; Rodríguez, B. Eur. J. Org. Chem. 1999, 1999, 2011–2015; (b) Crimmins, M. T.; Pace, J. M.; Nantermet, P. G.; Kim-Meade, A. S.; Thomas, J. B.; Watterson, S. H.; Wagman, A. S. *J. Am. Chem. Soc.* **1999**, *121*, 10249–10250.

(7) For examples of oxa-di-π-methane rearrangements of cyclohexadienones, see: (a) Barton, D. H. R.; de Mayo, P.; Shafiq, M. *J. Chem. Soc.* **1958**, 3314–3319; (b) Zimmerman, H. E.; Schuster, D. I. *J. Am. Chem. Soc.* **1961**, *83*, 4486–4488; (c) Zimmerman, H. E.; Swenton, J. S. *J. Am. Chem. Soc.* **1967**, *89*, 906–912; (d) Schuster, D. I.; Brisimitzakis, A. C. *J. Org. Chem.* **1987**, *52*, 3644–3649; (e) Pirrung, M. C.; Nunn, D. S. *Tetrahedron* **1996**, *52*, 5707–5738.

(8) Alvarez de Cienfuegos, L.; Mota, A. J.; Robles, R. *Org. Lett.* **2005**, *7*, 2161–2164.

(9) VanRheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, *17*, 1973–1976.

(10) Dueno, E. E.; Chu, F.; Kim, S.-I.; Jung, K. W. *Tetrahedron Lett.* **1999**, *40*, 1843–1846.

(11) Attempts to control the equivalents of the alkoxide nucleophile did not prove fruitful; in these reactions, an intractable mixture of products was observed.

(12) Trost, B. M.; Dong, G. *Chem. Eur. J.* **2009**, *15*, 6910–6919.

(13) Chen, K.; Richter, J. M.; Baran, P. S. *J. Am. Chem. Soc.* **2008**, *130*, 7247–7249.

(14) Abson, A.; Broom, N. J.; Coates, P. A.; Elder, J. S.; Forrest, A. K.; Hannan, P. C.; Hicks, A. J.; O'Hanlon, P. J.; Masson, N. D.; Pearson, N. D.; Pons, J. E.; Wilson, J. M. *J. Antibiot.* **1996**, *49*, 390–394.

(15) Hersel, U.; Steck, M.; Seifert, K. *Eur. J. Org. Chem.* **2000**, *2000*, 1609–1615.

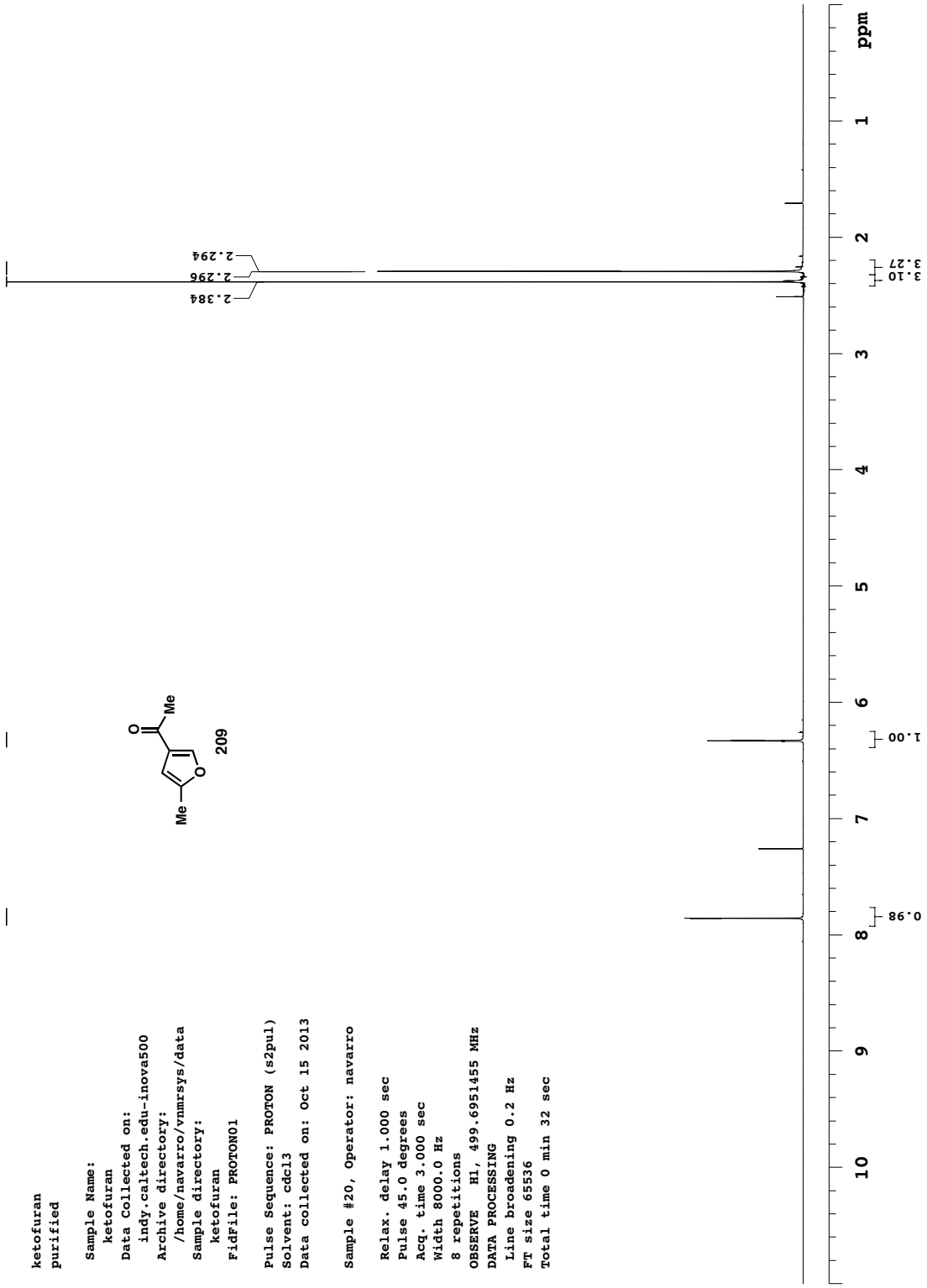
(16) Grignard reagent **214** was prepared as follows: To a suspension of magnesium turnings (1.60 g, 65.8 mmol) in THF (8 mL) was added diisobutylaluminum hydride (60 μL, 0.34 mmol). The resulting suspension was heated to reflux, and a solution of bromide **S16** (7.58 g, 40.1 mmol) in THF (42 mL) was added dropwise. The reaction was maintained at reflux for 1 hour, then cooled to room temperature. The resulting Grignard reagent was titrated and stored in a Schlenk tube.

(17) Less than 1 mg of analytically pure dihydrofuran **206** was isolated; as such, some carbon signals were extrapolated from HMBC spectral data. See Appendix 3.

APPENDIX 3

Spectra Relevant to Chapter 4:

Progress Toward the Total Synthesis of Acutumine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ketofuran
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Pulse 45.0 degrees
Acq. time 3.000 sec
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Line broadening 0.2 Hz
FT size 65536
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Me
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Me
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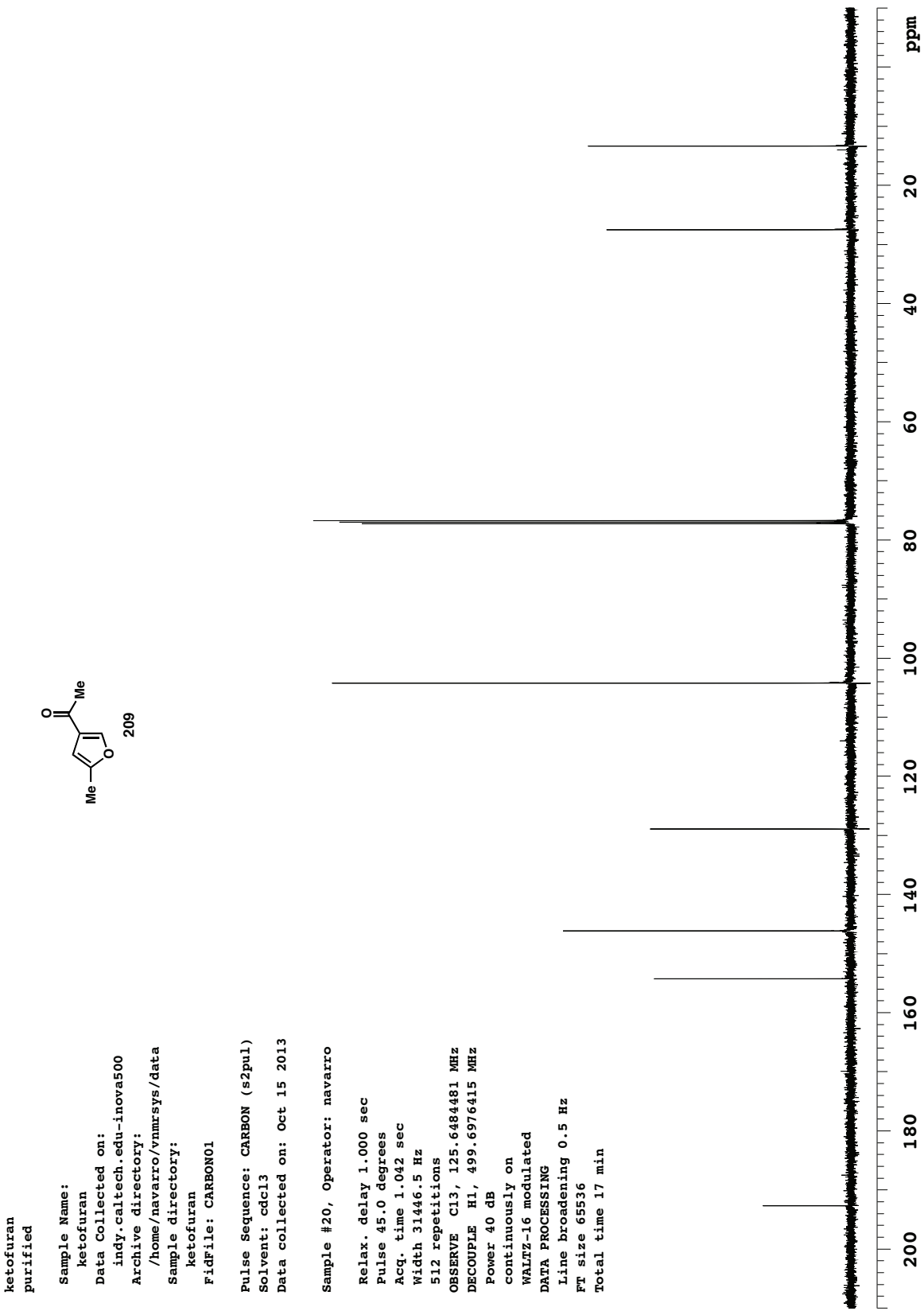
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DECOUPLE H1, 499.6976415 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
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160
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120
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80
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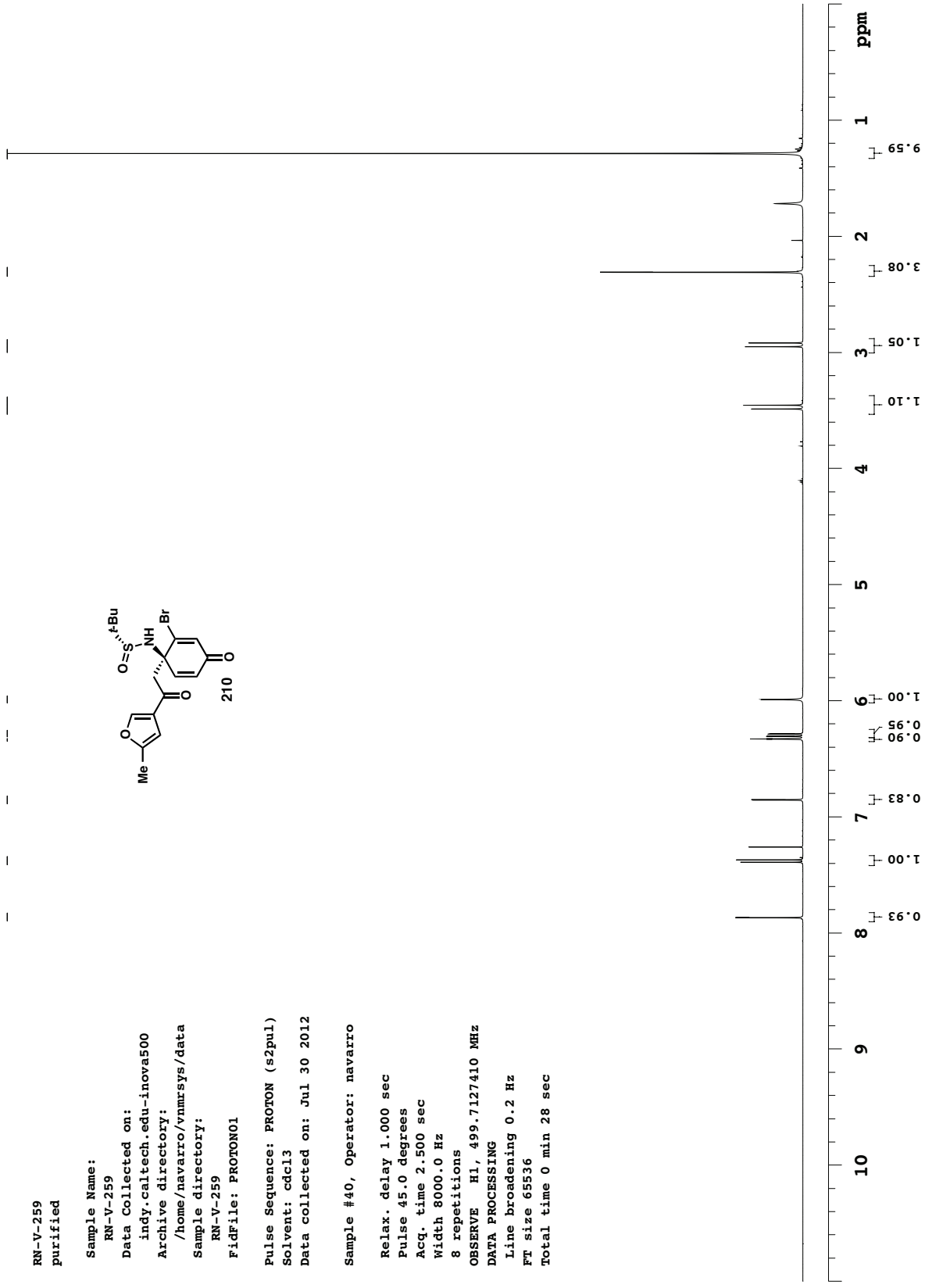
40
20
ppm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Width 8000.0 Hz
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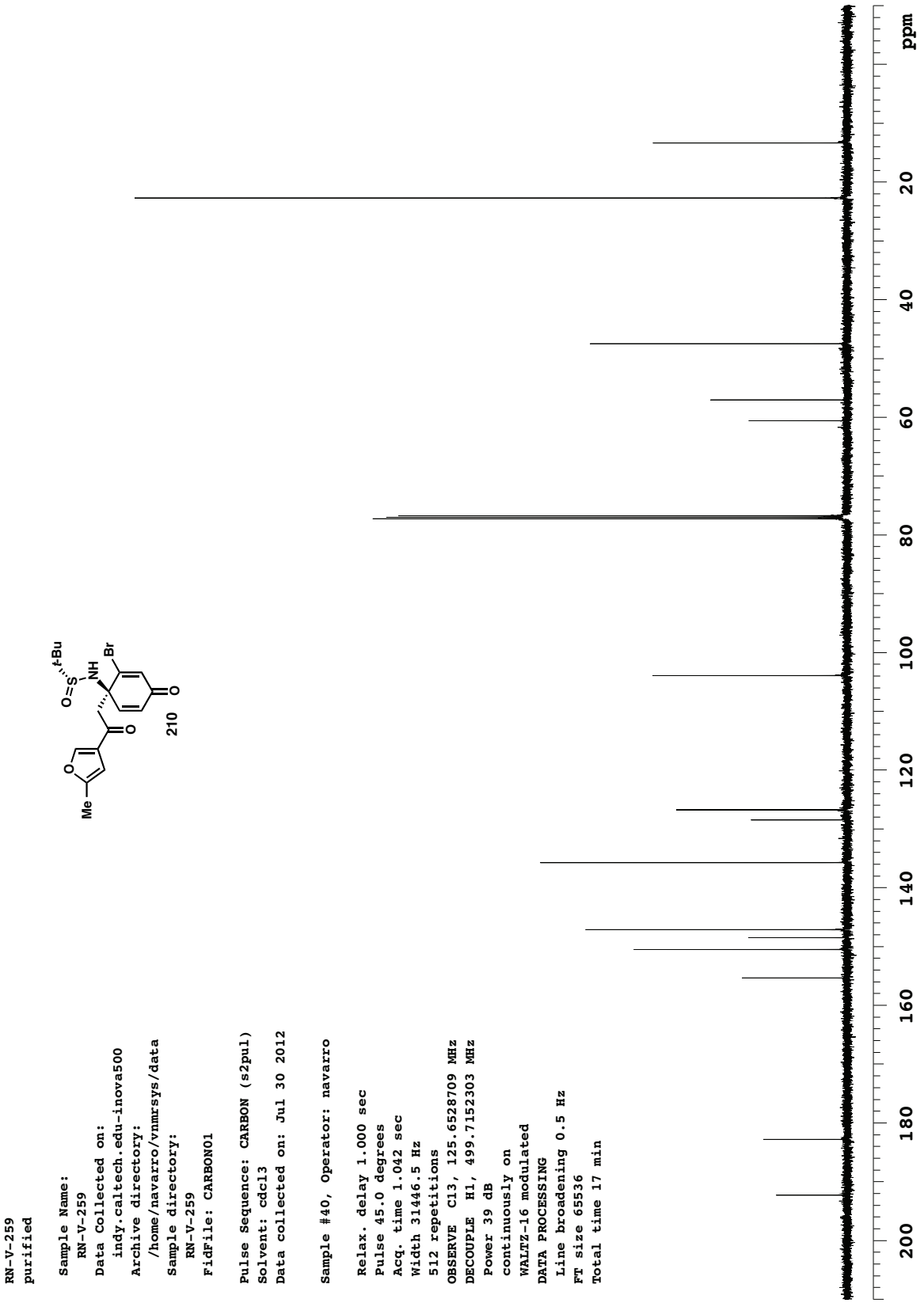
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continuously on
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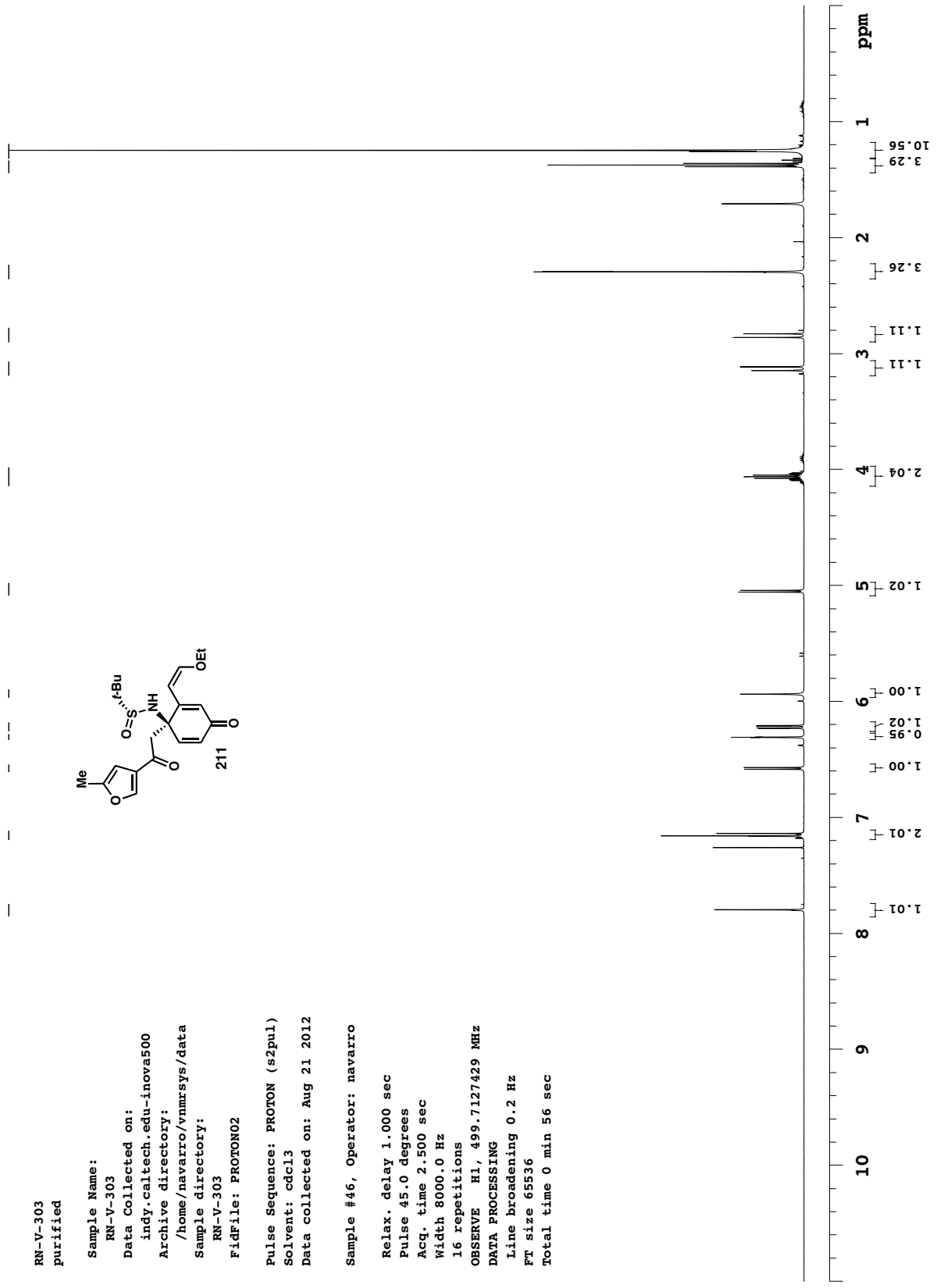
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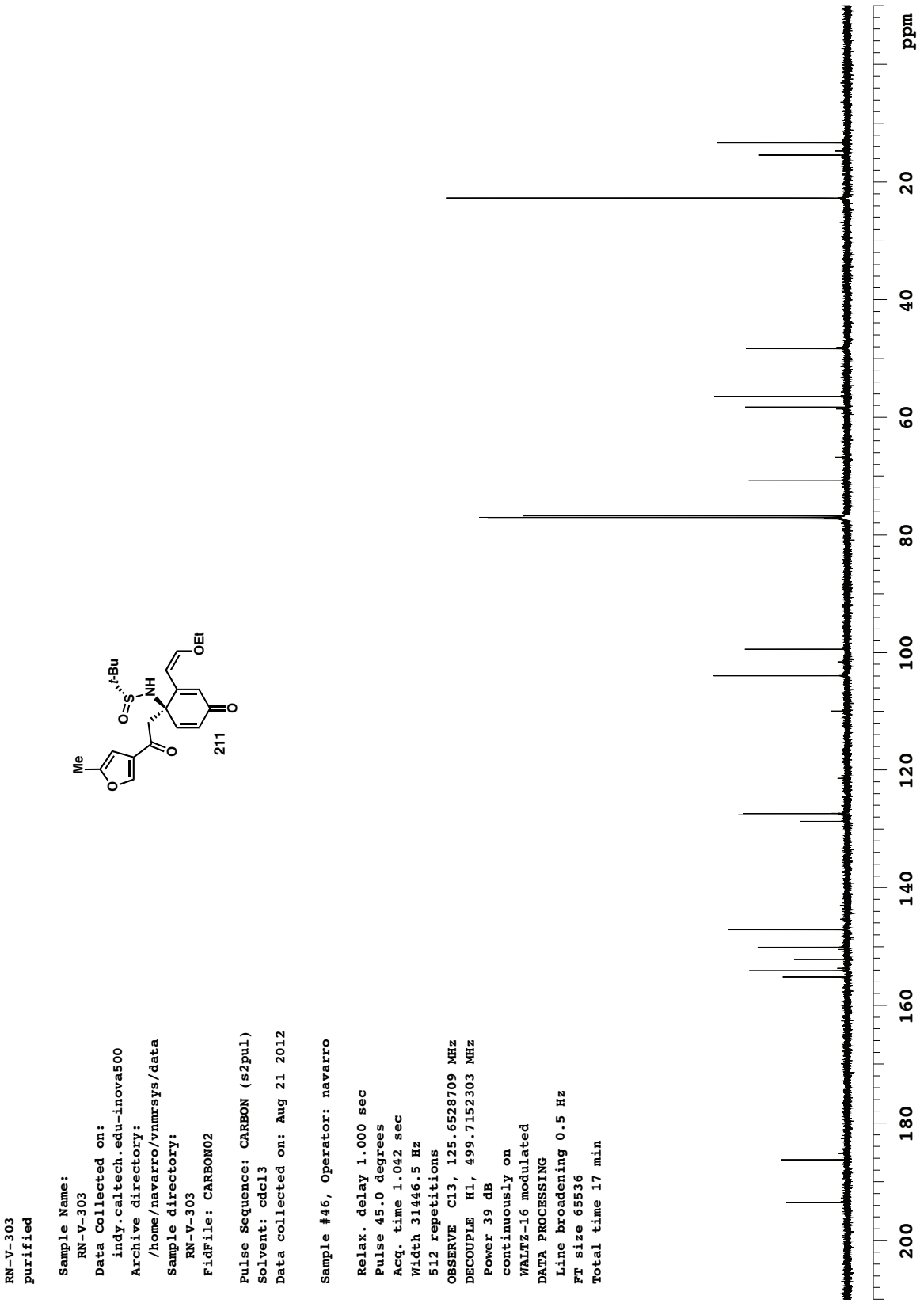
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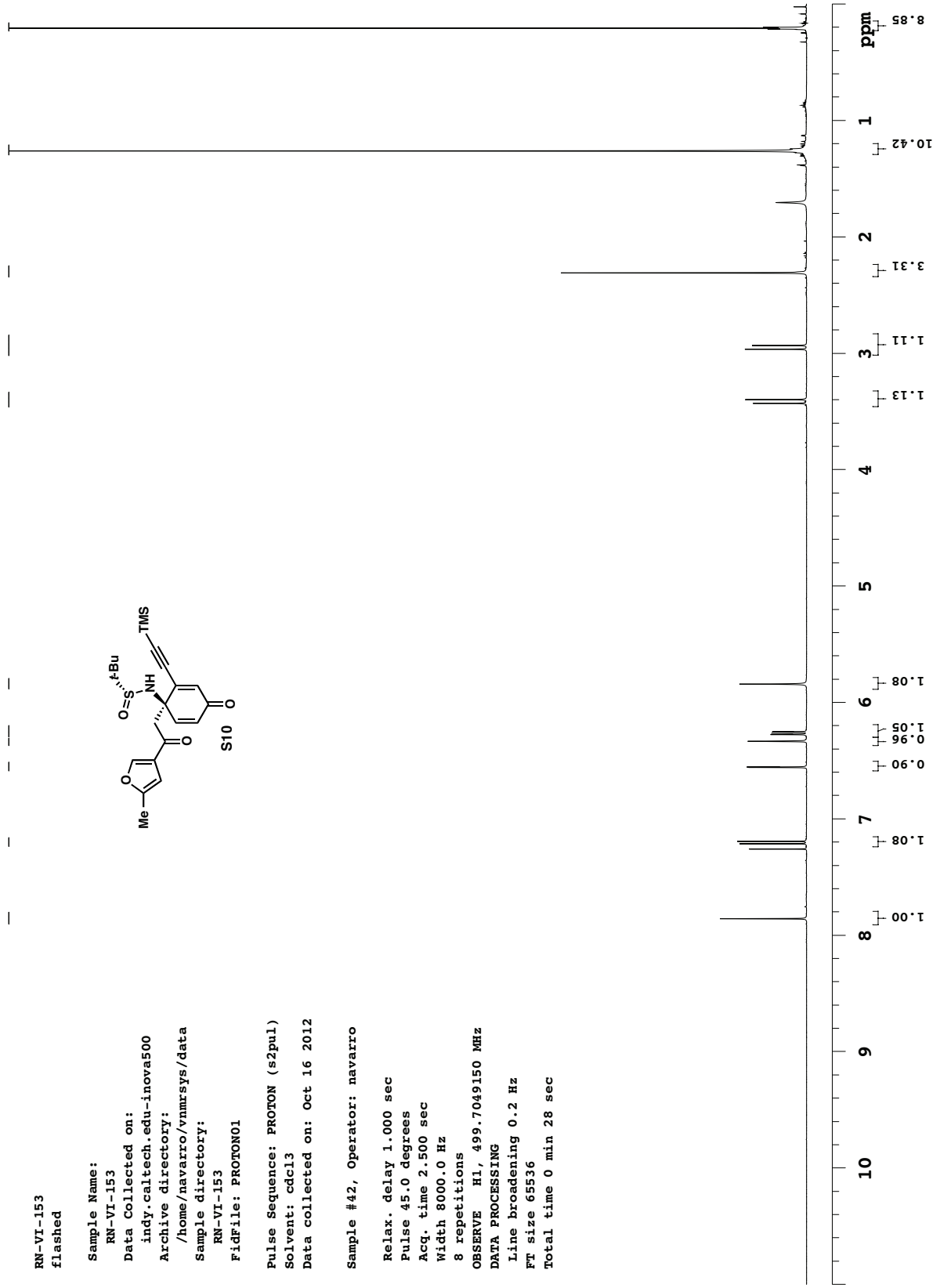
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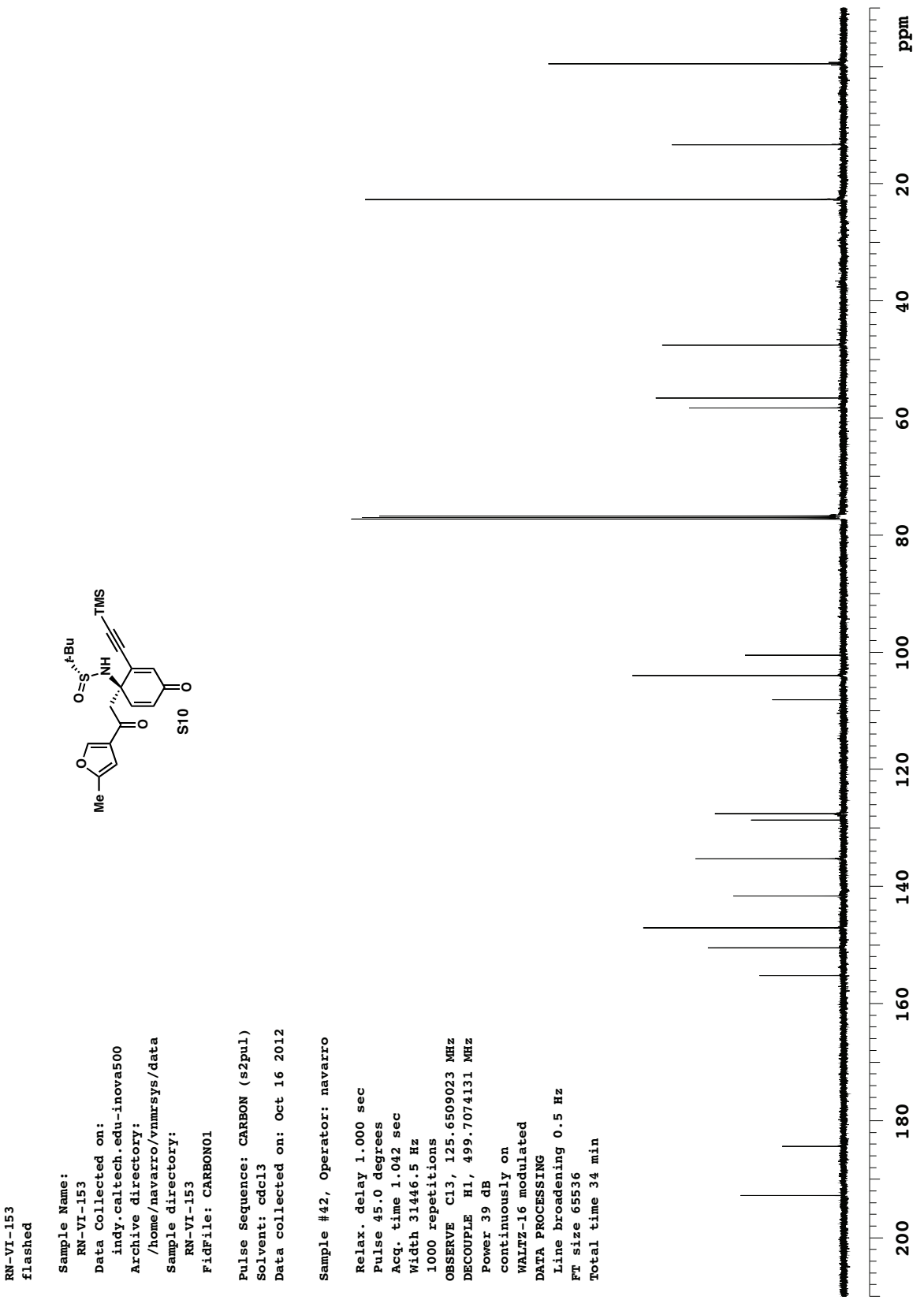
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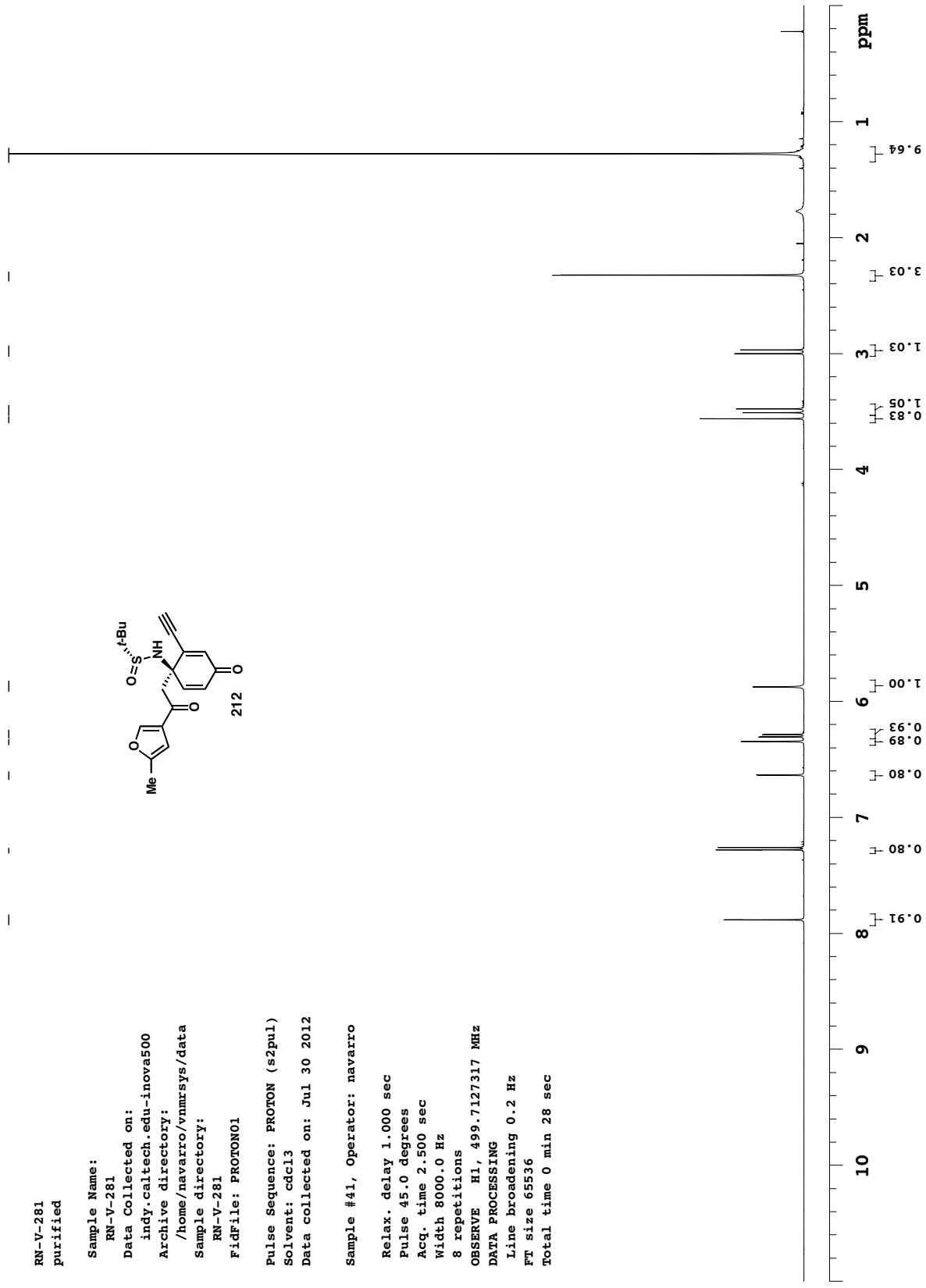
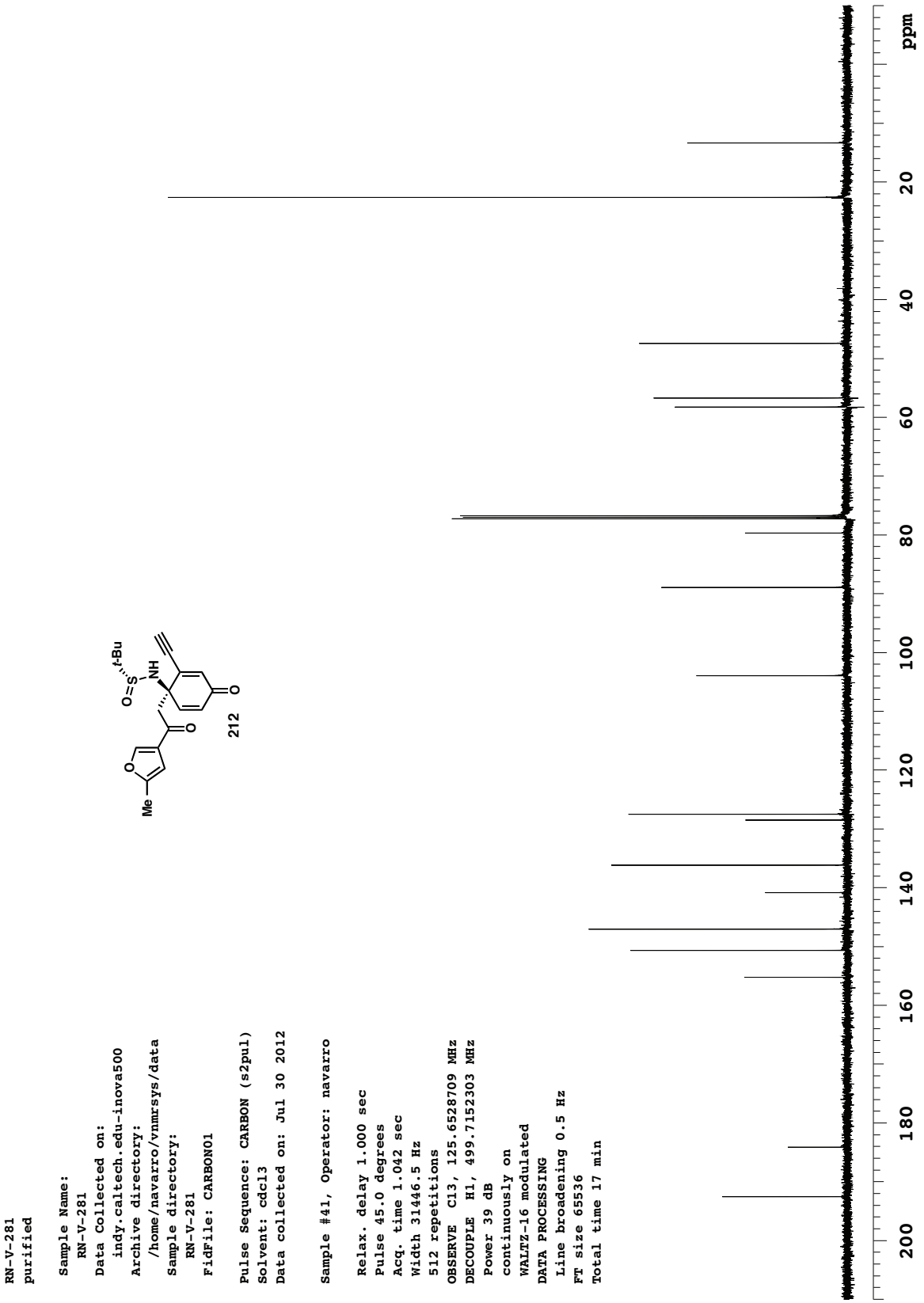
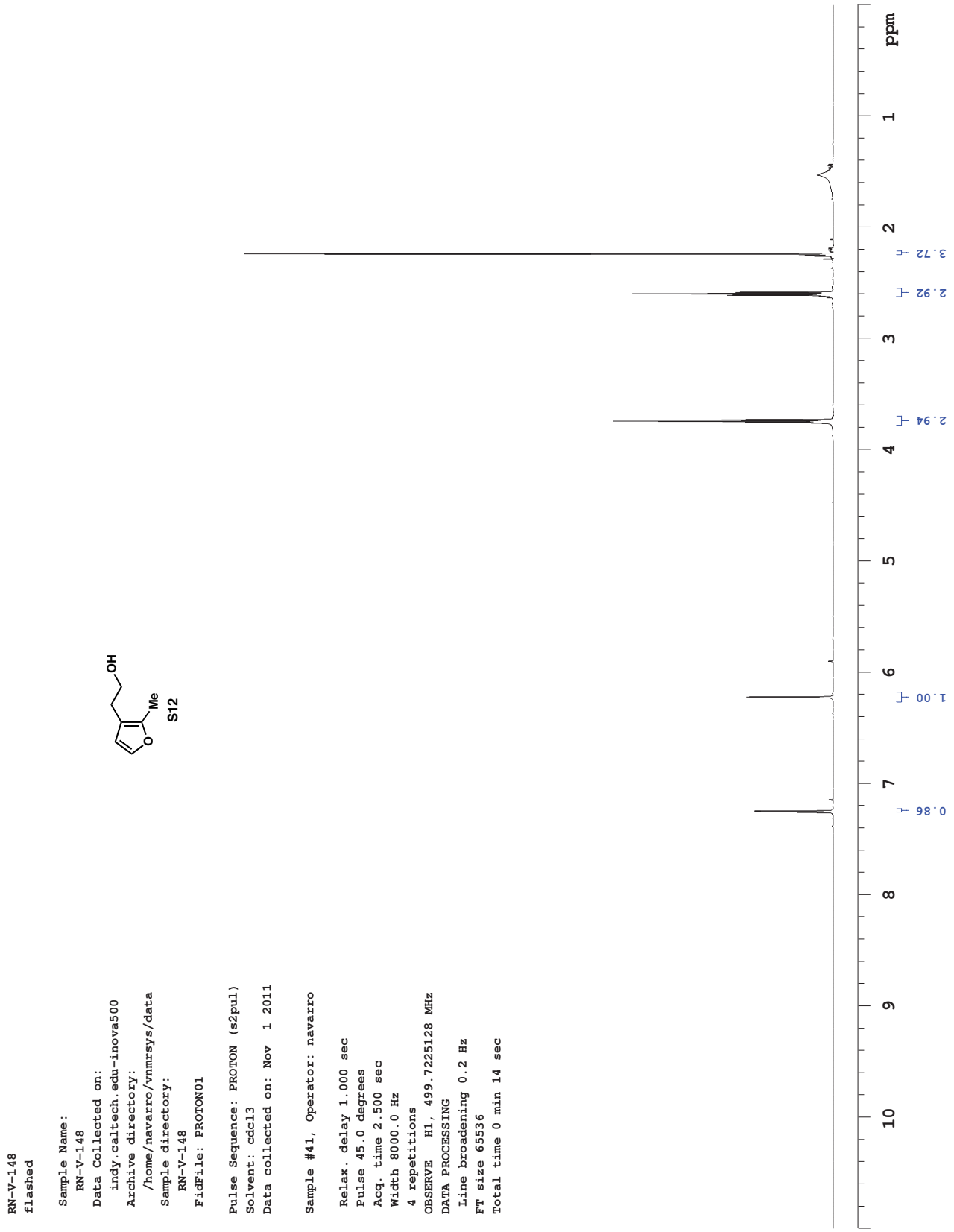
RN-VI-153
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-153
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 16 2012
Sample #42, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6509023 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
S10
TMS
t-Bu
NH
Me
ppm
200
180
160
140
120
100
80
60
40
20


RN-V-281
purified
Sample Name:
RN-V-281
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-281
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jul 30 2012
Sample #41, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7127317 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 28 sec
t-Bu
NH
O
Me
212
ppm
9.64
3.03
1.03
0.83
1.05
1.00
0.89
0.93
0.80
0.80
0.91


RN-V-281
purified
Sample Name:
RN-V-281
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-281
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 30 2012
Sample #41, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528709 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
212
ppm
200
180
160
140
120
100
80
60
40
20


RN-V-148
flashed
Sample Name:
RN-V-148
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-148
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Nov 1 2011
Sample #41, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
4 repetitions
OBSERVE H1, 499.7225128 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 14 sec
OH
Me
O
S12
3.72
2.92
2.94
1.00
0.86
ppm

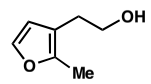
RN-V-148
flashed

Sample Name:
RN-V-148
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-148
FidFile: CARBON01

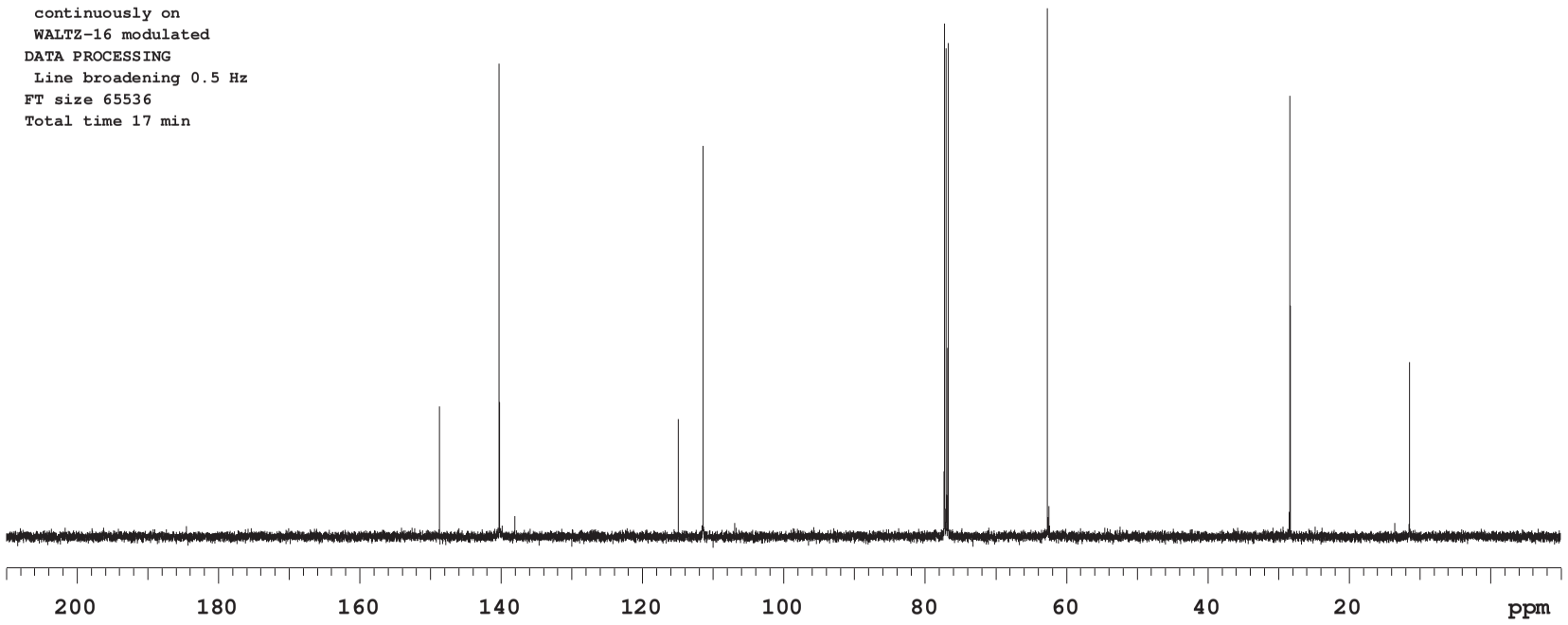
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Nov 1 2011

Sample #41, Operator: navarro

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6553281 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min



S12



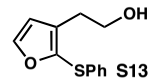
RN-VI-55
flashed

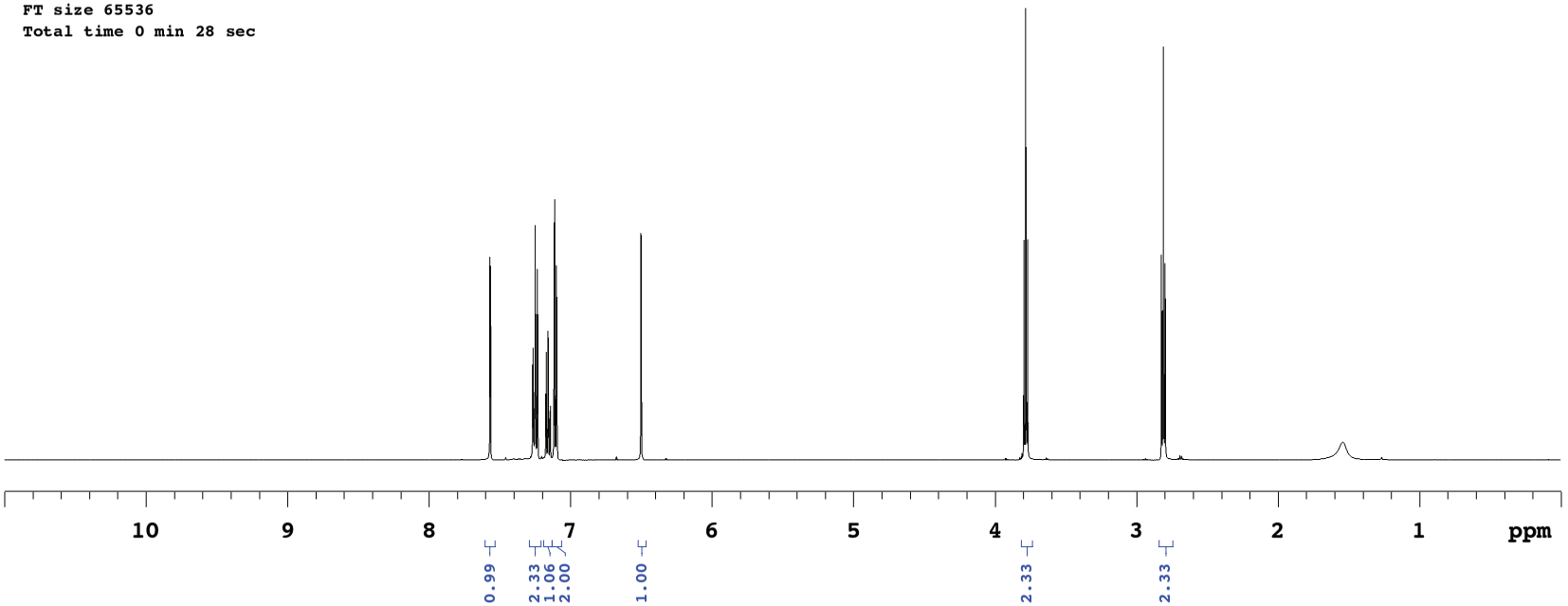
Sample Name:
RN-VI-55
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-55
FidFile: PROTON01

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 6 2012

Sample #41, Operator: navarro

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7127369 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 28 sec





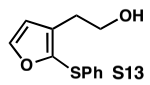
RN-VI-55
flashed

Sample Name:
RN-VI-55
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-55
FidFile: CARBON01

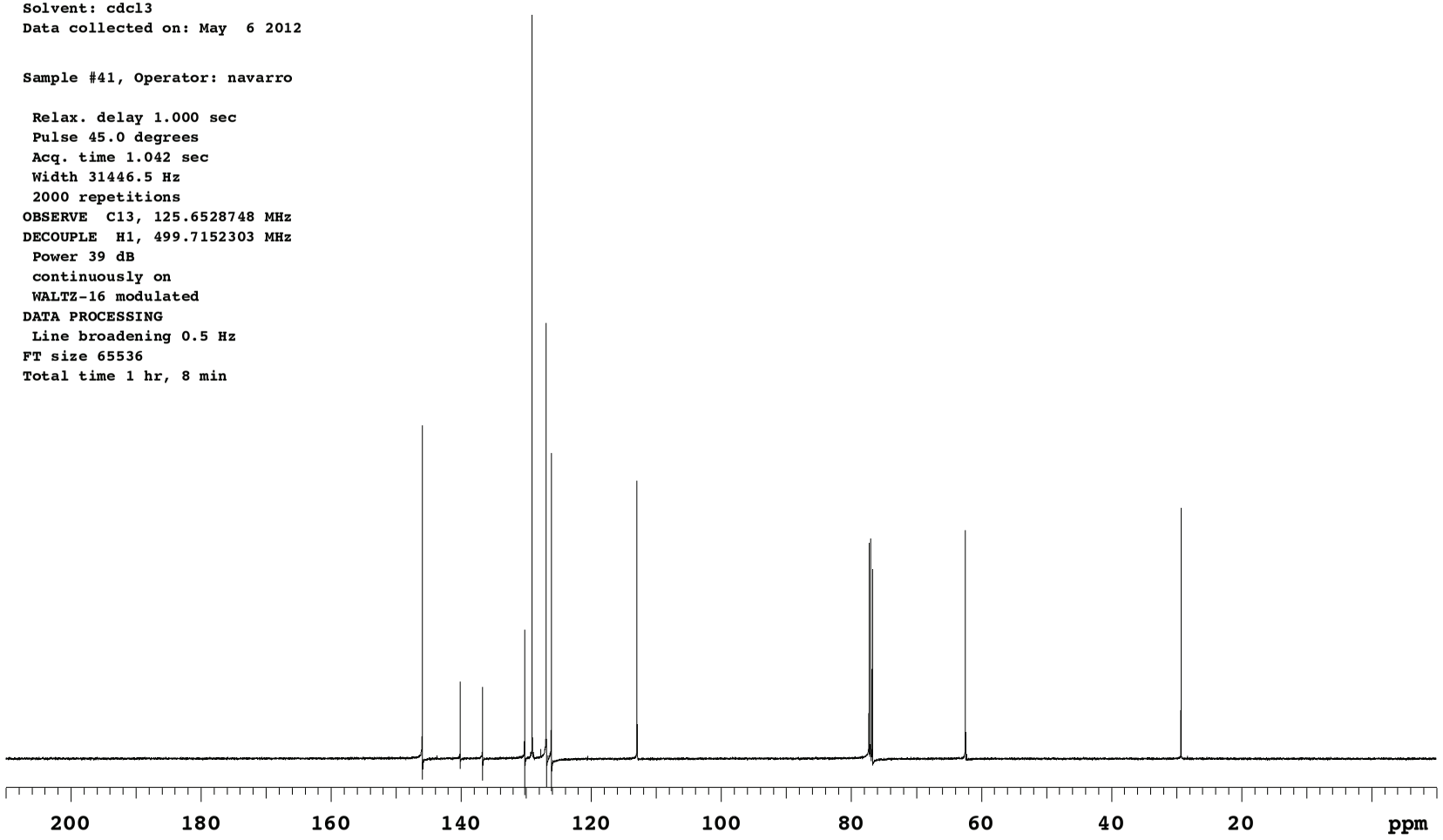
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 6 2012

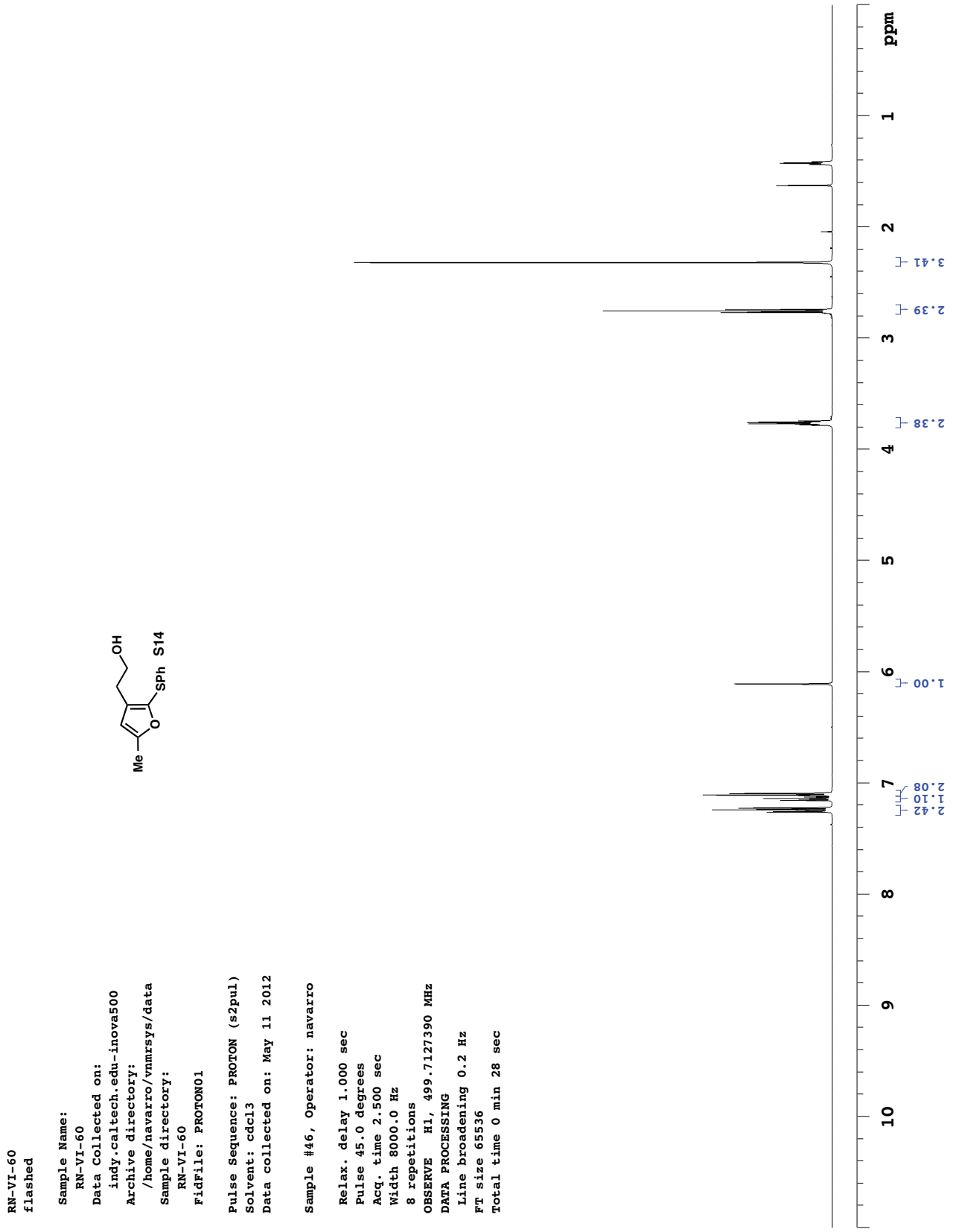
Sample #41, Operator: navarro

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2000 repetitions
OBSERVE C13, 125.6528748 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 8 min



S13




RN-VI-60
flashed
Sample Name:
RN-VI-60
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-60
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 11 2012
Sample #46, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7127390 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 28 sec
OH
SPh
S14
Me
O
ppm
10
9
8
7
6
5
4
3
2
1
2.42
1.10
2.08
1.00
2.38
2.39
3.41

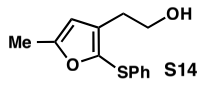
RN-VI-60
flashed

Sample Name:
RN-VI-60
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-60
FidFile: CARBON01

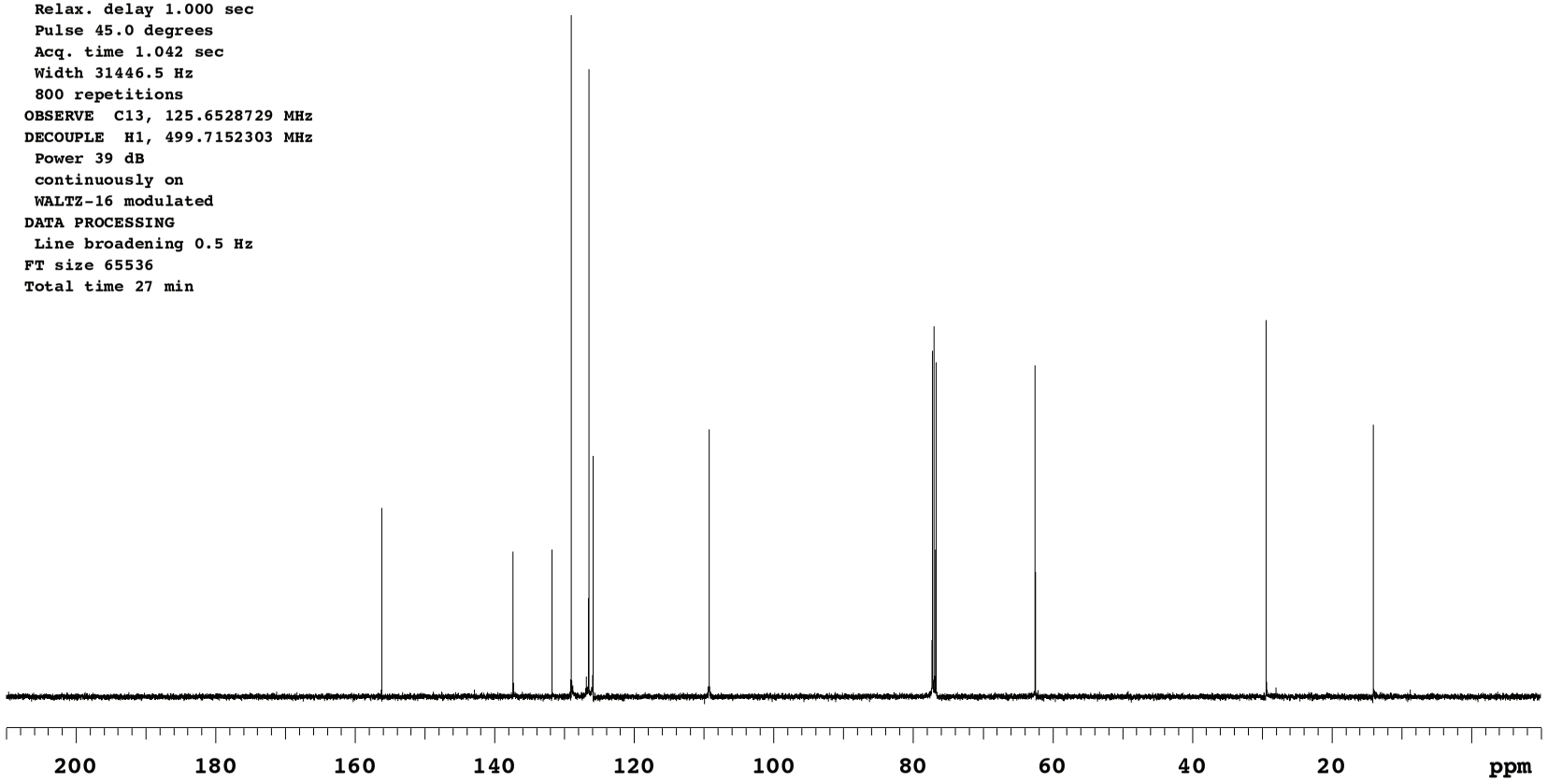
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 11 2012

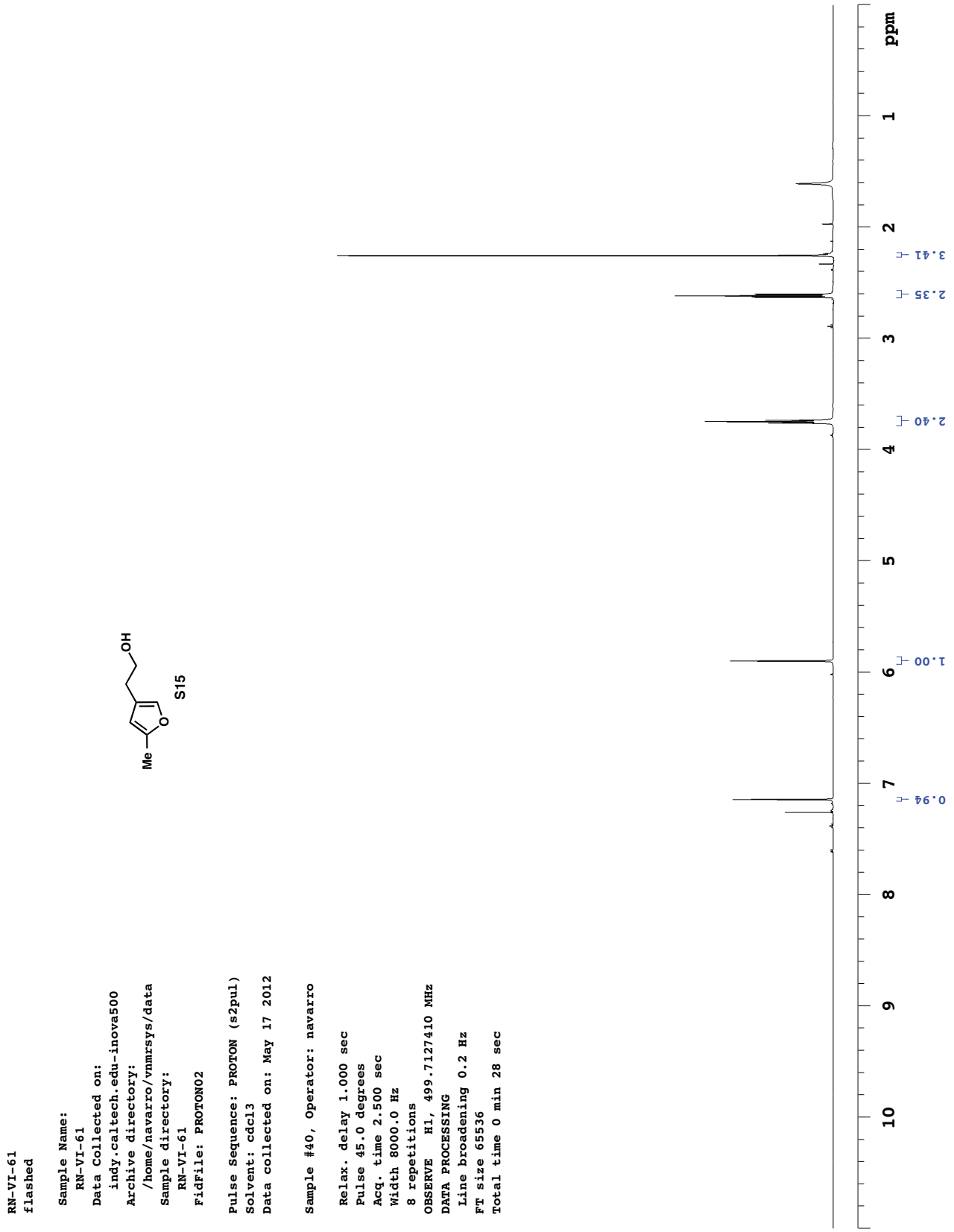
Sample #46, Operator: navarro

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
800 repetitions
OBSERVE C13, 125.6528729 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 27 min



S14




RN-VI-61
flashed
Sample Name:
RN-VI-61
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-61
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 17 2012
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7127410 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 28 sec
OH
Me
O
S15
0.94
1.00
2.40
2.35
3.41
ppm
10
9
8
7
6
5
4
3
2
1

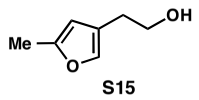
RN-VI-61
flashed

Sample Name:
RN-VI-61
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-61
FidFile: CARBON02

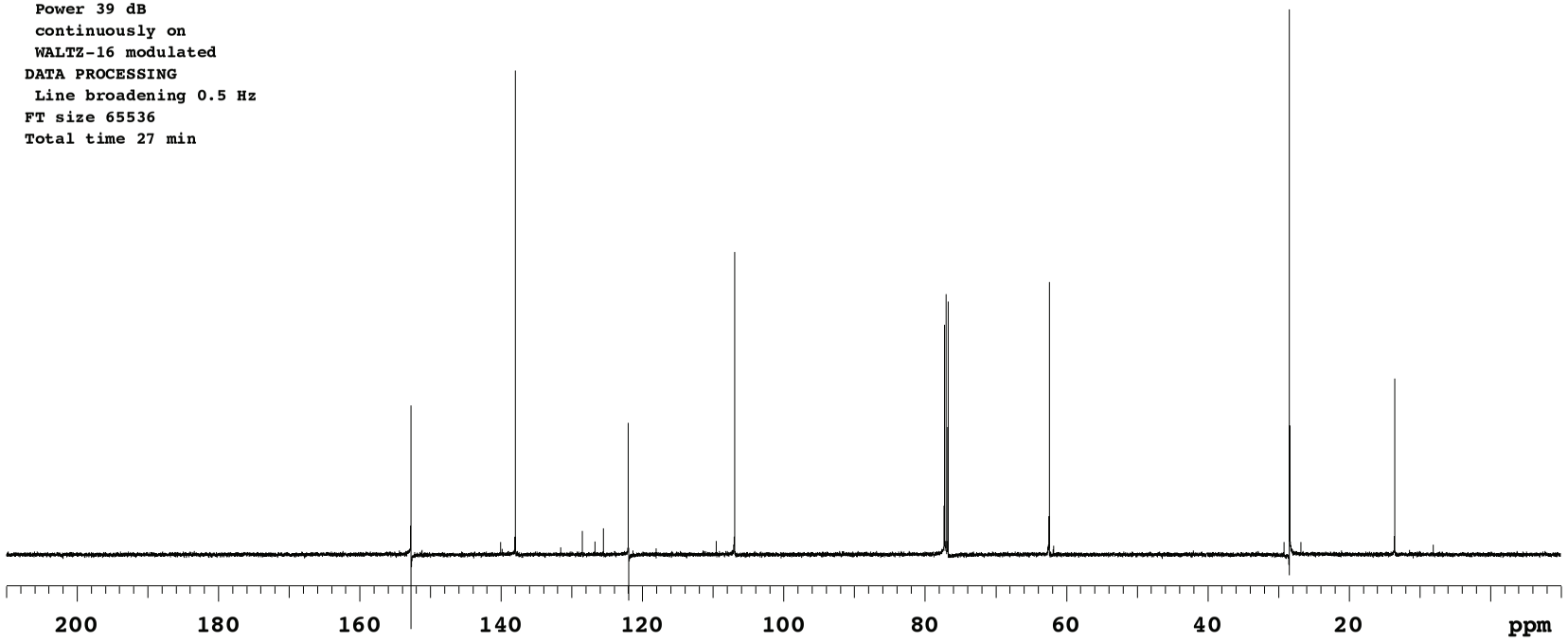
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 17 2012

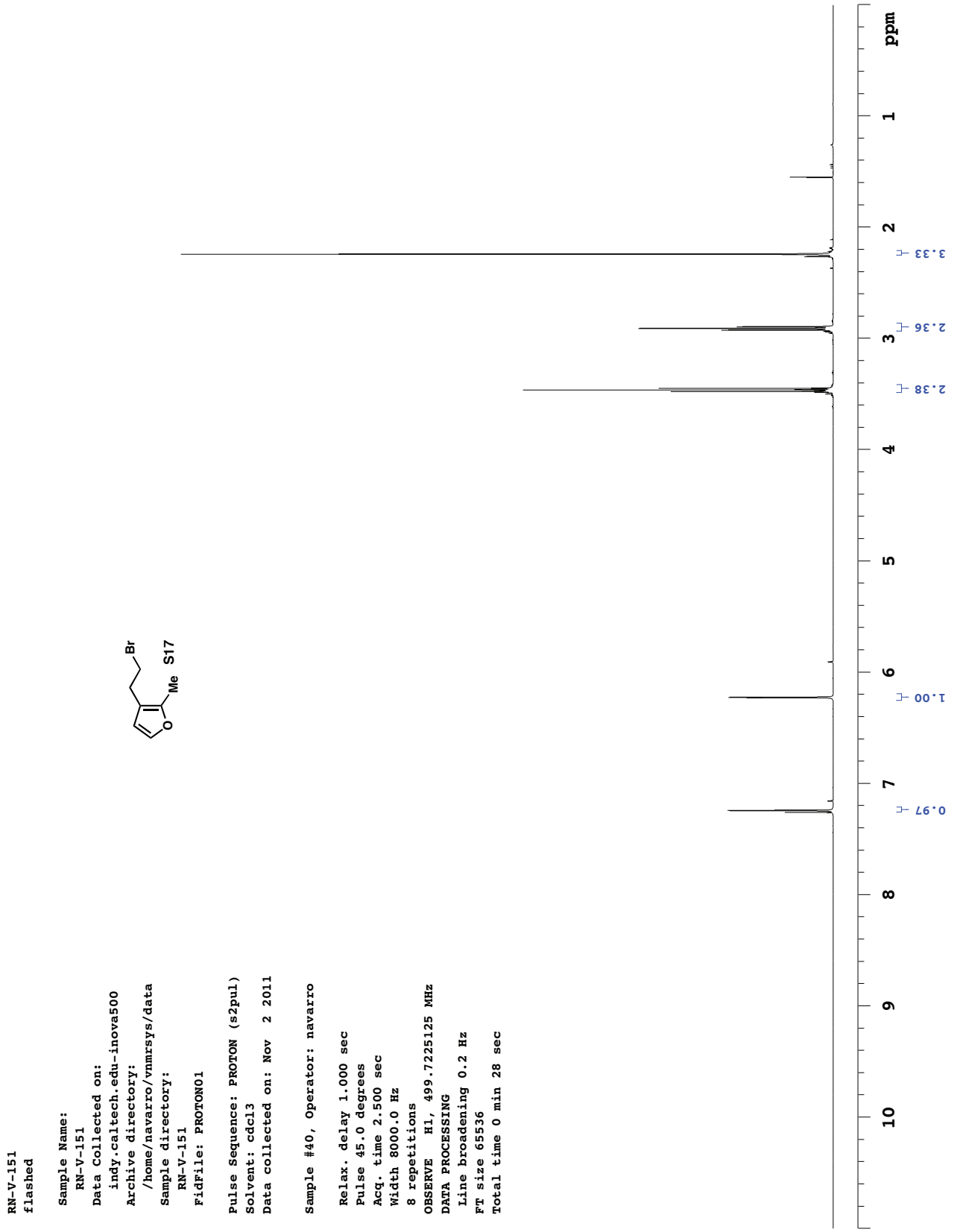
Sample #40, Operator: navarro

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
800 repetitions
OBSERVE C13, 125.6528729 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 27 min



S15




RN-V-151
flashed
Sample Name:
RN-V-151
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-151
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Nov 2 2011
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7225125 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 28 sec
Br
Me
O
S17
ppm
10
9
8
7
6
5
4
3
2
1
0.97
1.00
2.38
2.36
3.33

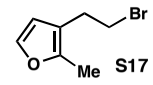
RN-V-151
flashed

Sample Name:
RN-V-151
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-151
FidFile: CARBON01

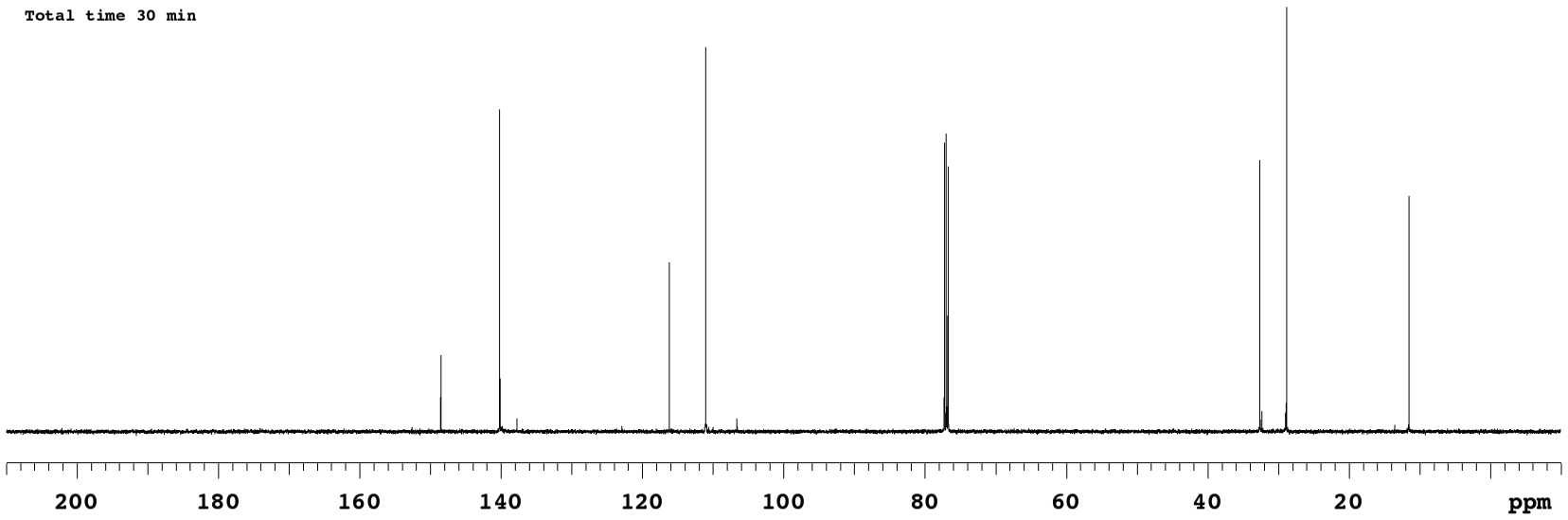
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Nov 2 2011

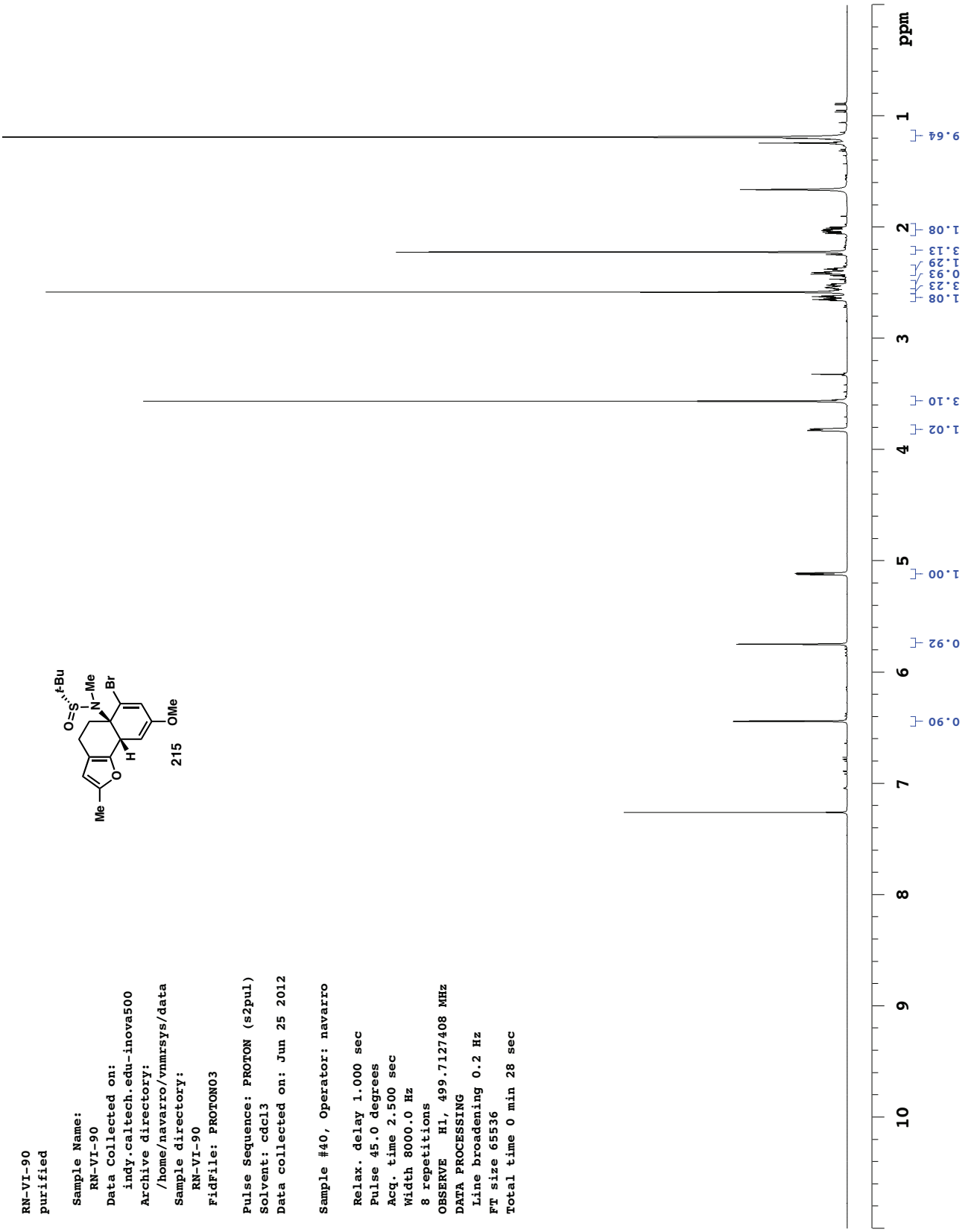
Sample #40, Operator: navarro

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
900 repetitions
OBSERVE C13, 125.6553291 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 30 min



S17




RN-VI-90
purified
Sample Name:
RN-VI-90
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-90
FidFile: PROTON03
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 25 2012
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7127408 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 28 sec
O=S
t-Bu
N
Me
Br
H
O
Me
OMe
215
ppm
1
2
3
4
5
6
7
8
9
10
9.64
1.08
3.13
1.29
0.93
3.23
1.08
3.10
1.02
1.00
0.92
0.90

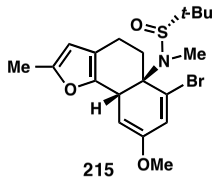
RN-VI-90
purified

Sample Name:
RN-VI-90
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-90
FidFile: CARBON02

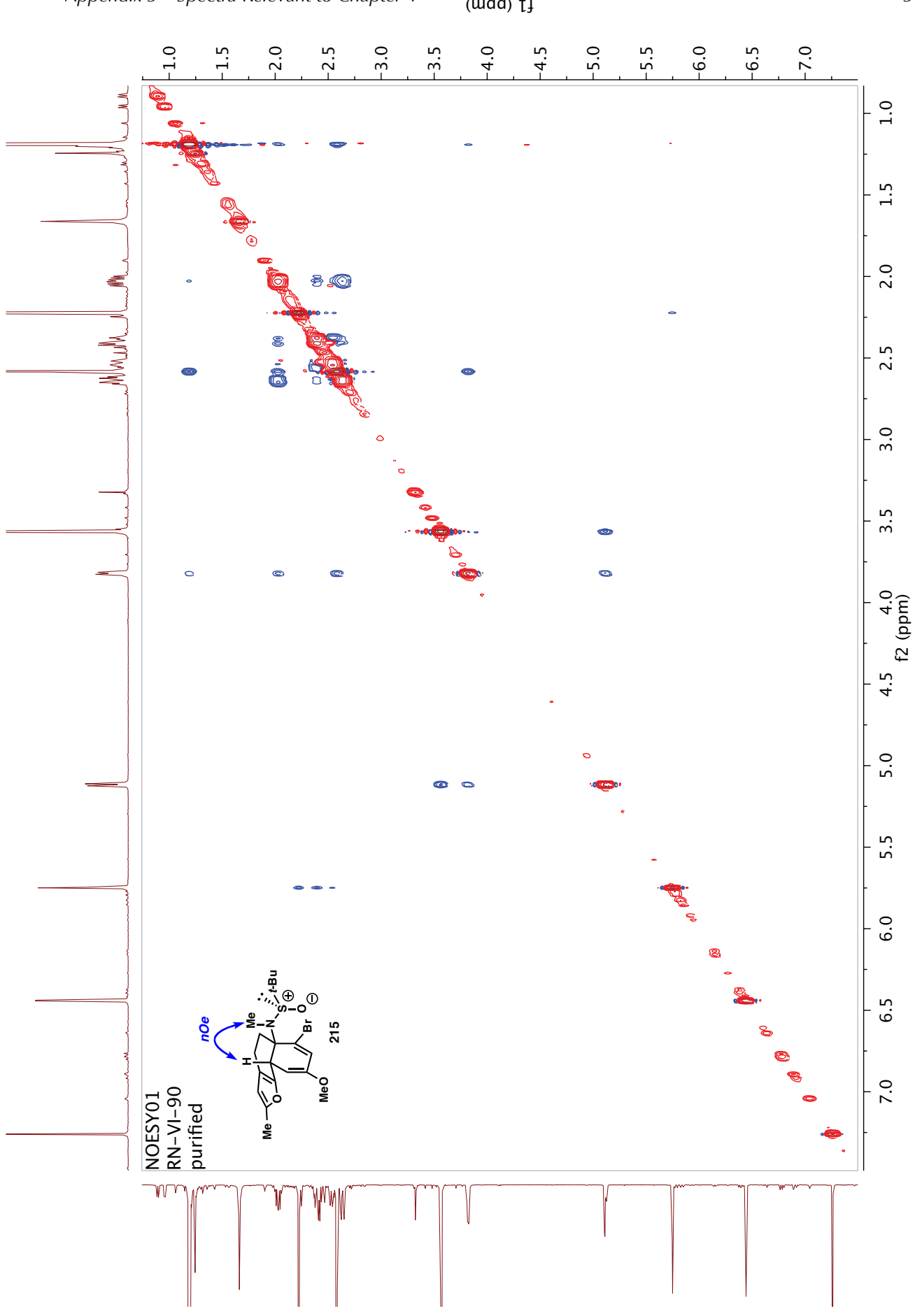
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 25 2012

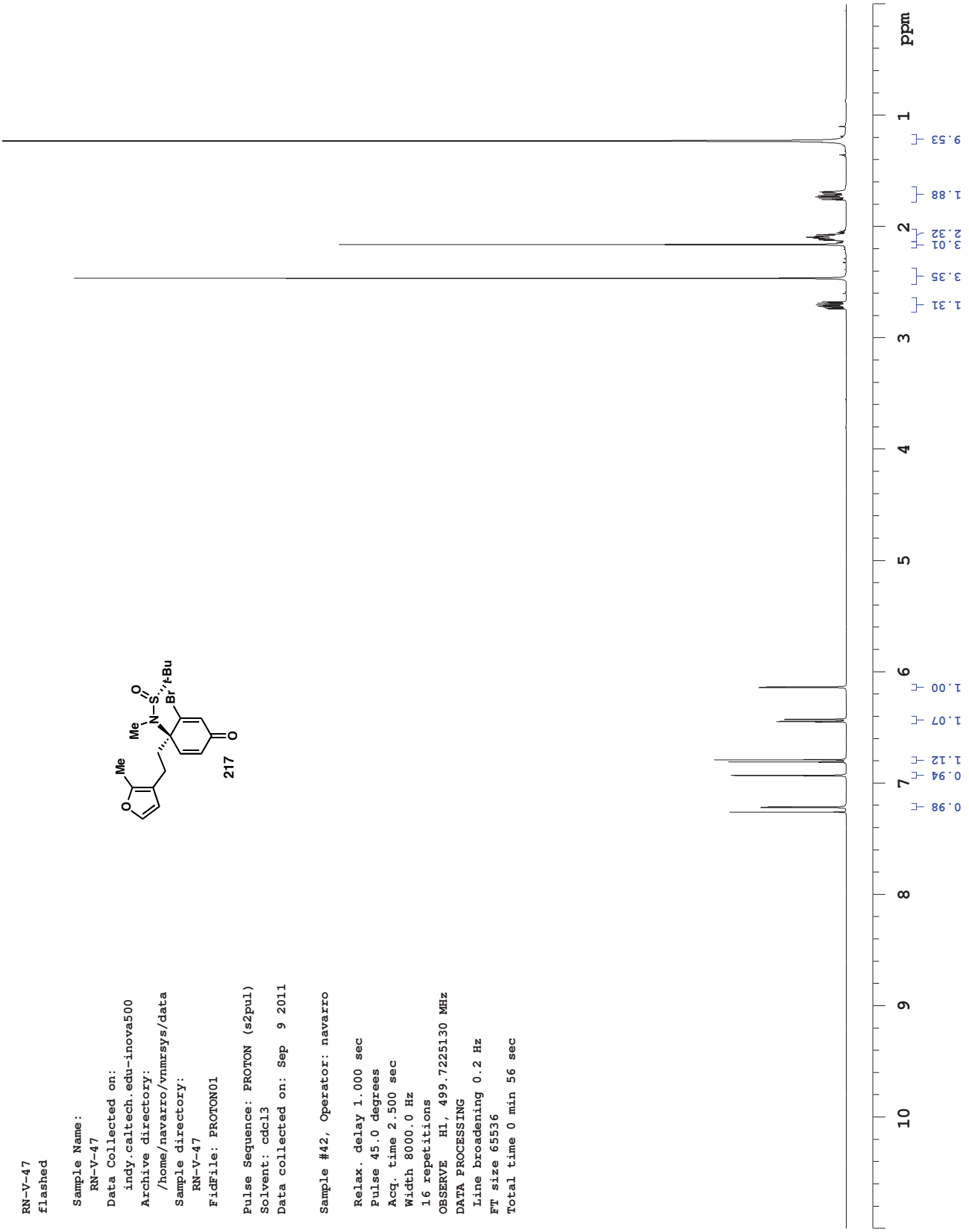
Sample #40, Operator: navarro

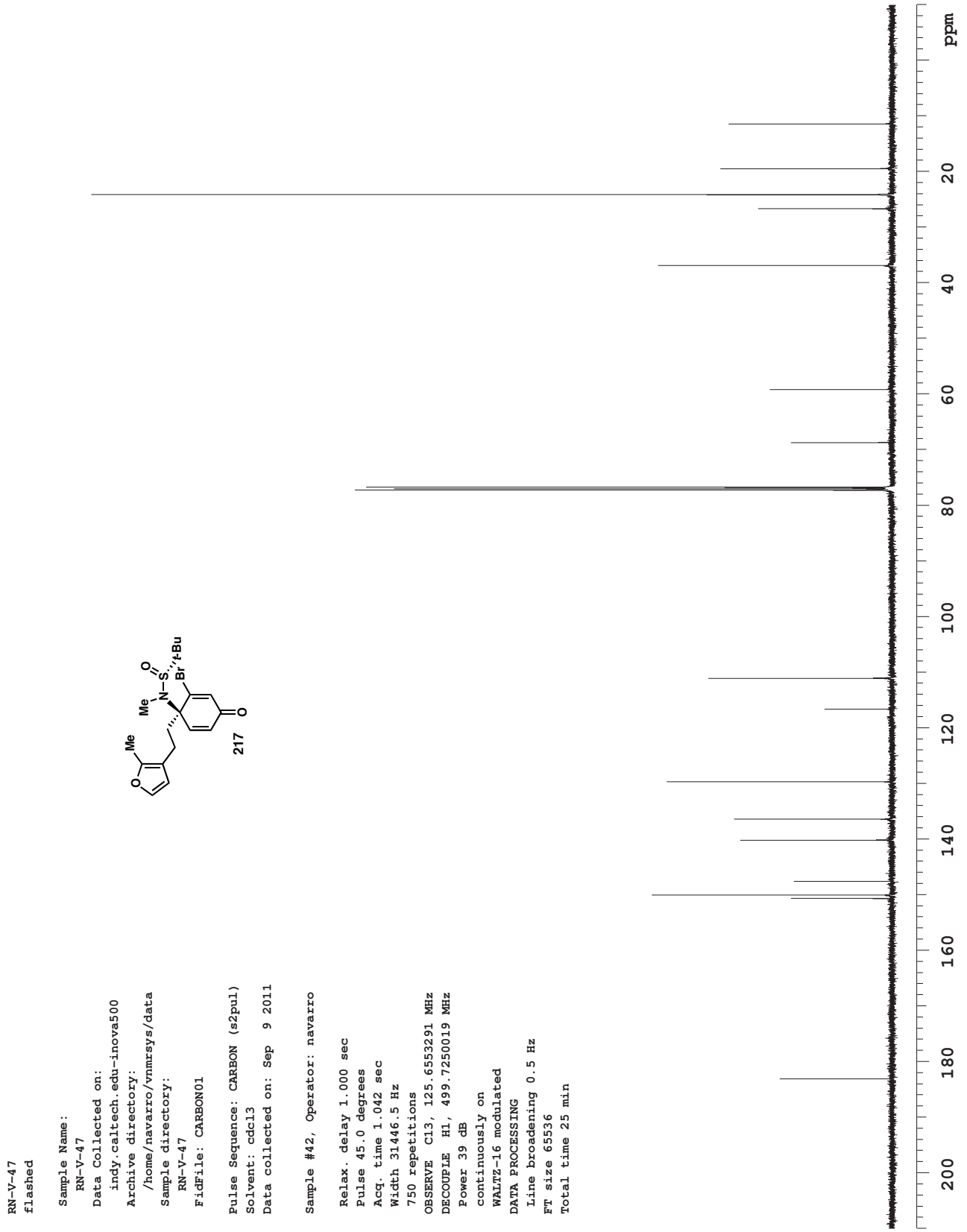
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6528710 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min

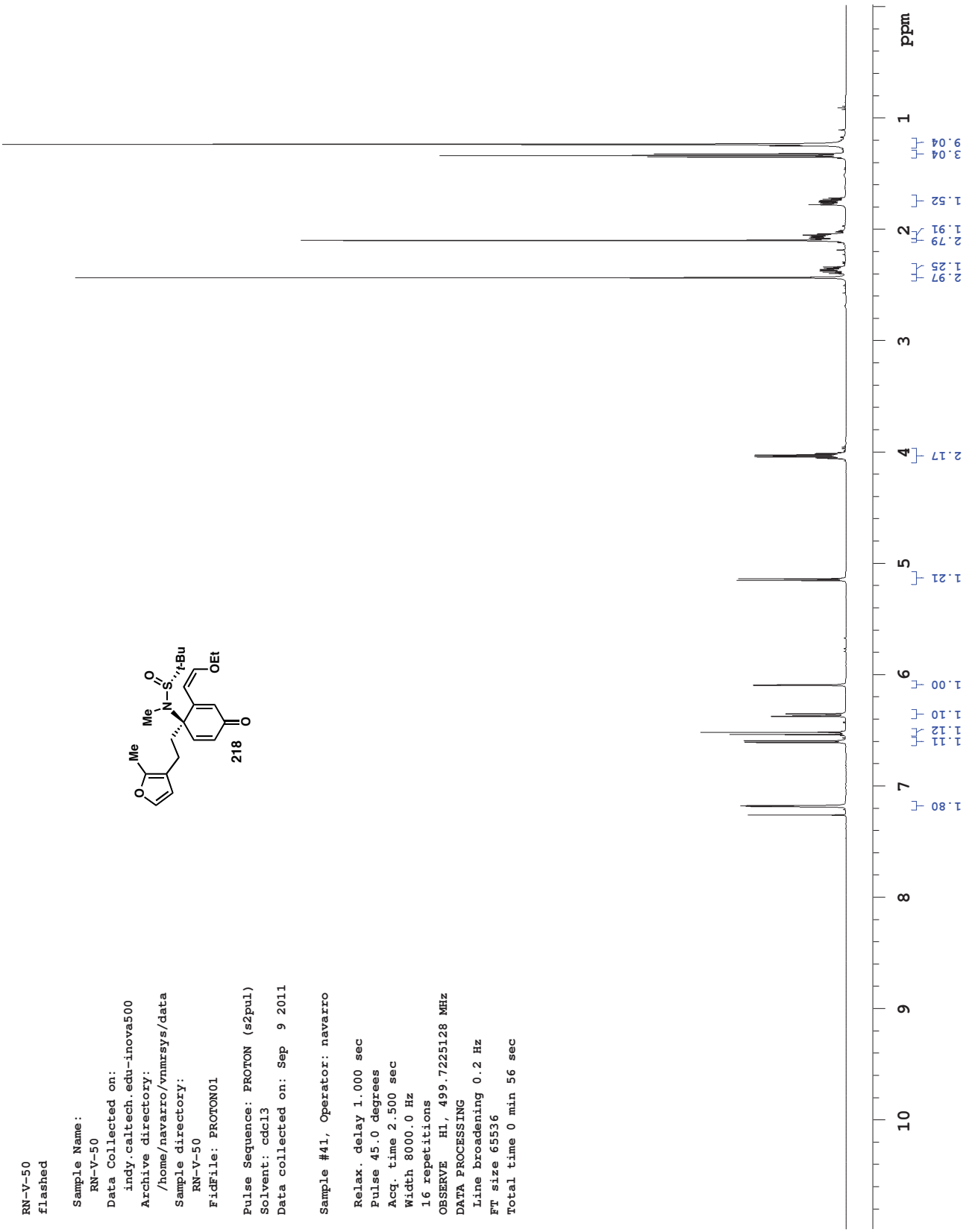


215


f1 (ppm)
f2 (ppm)
NOESY01
RN-VI-90
purified
nOe
215
Me
H
O
Me
N
S
t-Bu
O
Br
MeO


RN-V-47
flashed
Sample Name:
RN-V-47
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-47
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 9 2011
Sample #42, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7225130 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 56 sec
Me
O
N
S
O
Br
tBu
Me
O
O
217
ppm
1
2
3
4
5
6
7
8
9
10
9.53
1.88
2.32
3.01
3.35
1.31
1.00
1.07
1.12
0.94
0.98


RN-V-47
flashed
Sample Name:
RN-V-47
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-47
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 9 2011
Sample #42, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
750 repetitions
OBSERVE C13, 125.6553291 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 25 min
Me
Me
O
N
S
Br
t-Bu
O
O
Me
217
200
180
160
140
120
100
80
60
40
20
ppm


RN-V-50
flashed
Sample Name:
RN-V-50
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-50
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 9 2011
Sample #41, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7225128 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 56 sec
Me
Me
t-Bu
OEt
218
ppm
9.04
3.04
1.52
1.91
2.79
1.25
2.97
2.17
1.21
1.00
1.10
1.12
1.11
1.80

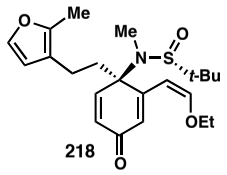
RN-V-50
flashed

Sample Name:
RN-V-50
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-50
FidFile: CARBON01

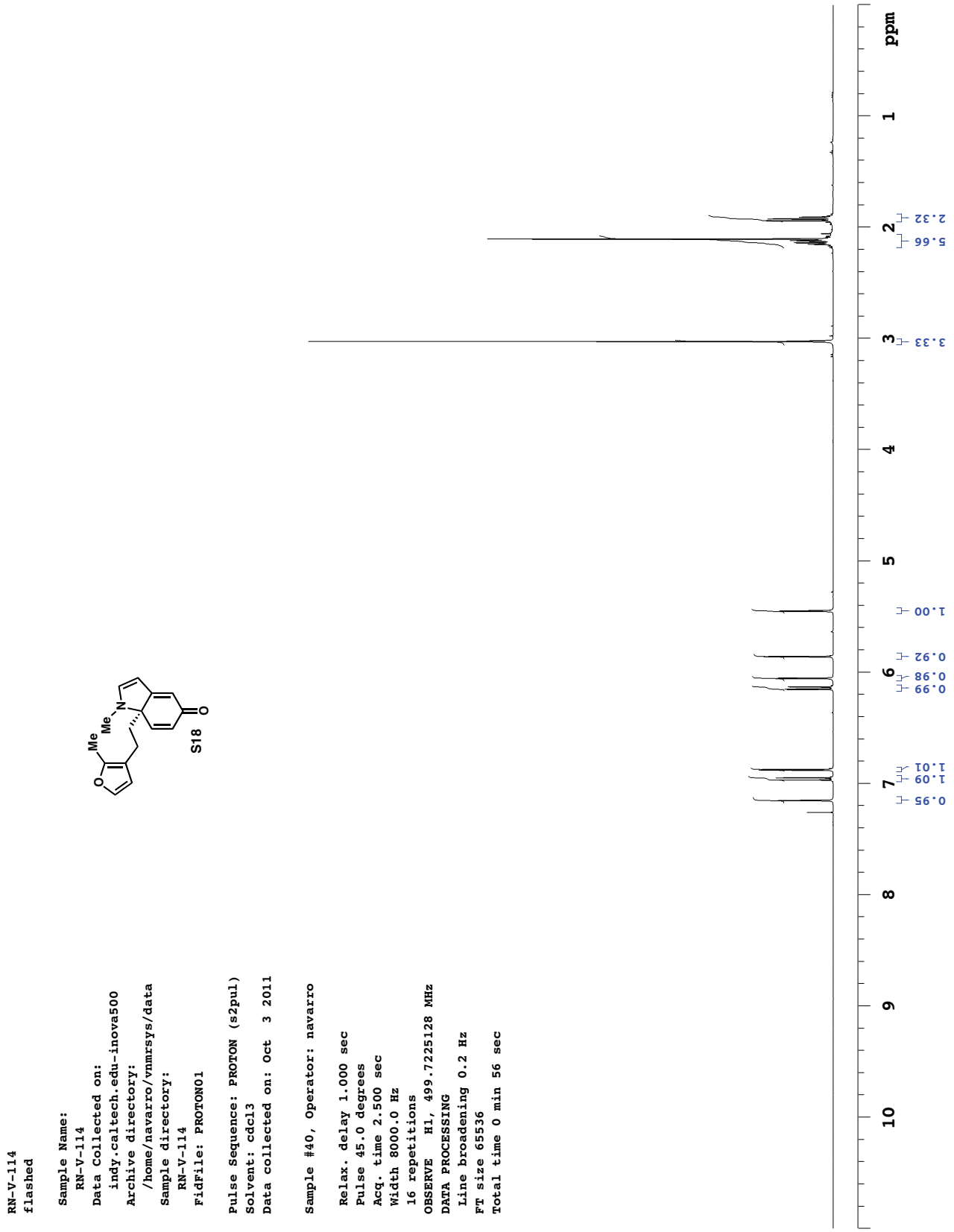
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 9 2011

Sample #41, Operator: navarro

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
750 repetitions
OBSERVE C13, 125.6553300 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 25 min



218


RN-V-114
flashed
Sample Name:
RN-V-114
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-114
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 3 2011
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7225128 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 56 sec
Me
Me
N
O
O
S18
ppm
10
9
8
7
6
5
4
3
2
1
0.95
1.09
1.01
0.92
0.98
0.99
1.00
3.33
5.66
2.32

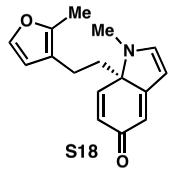
RN-V-114
flashed

Sample Name:
RN-V-114
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-114
FidFile: CARBON01

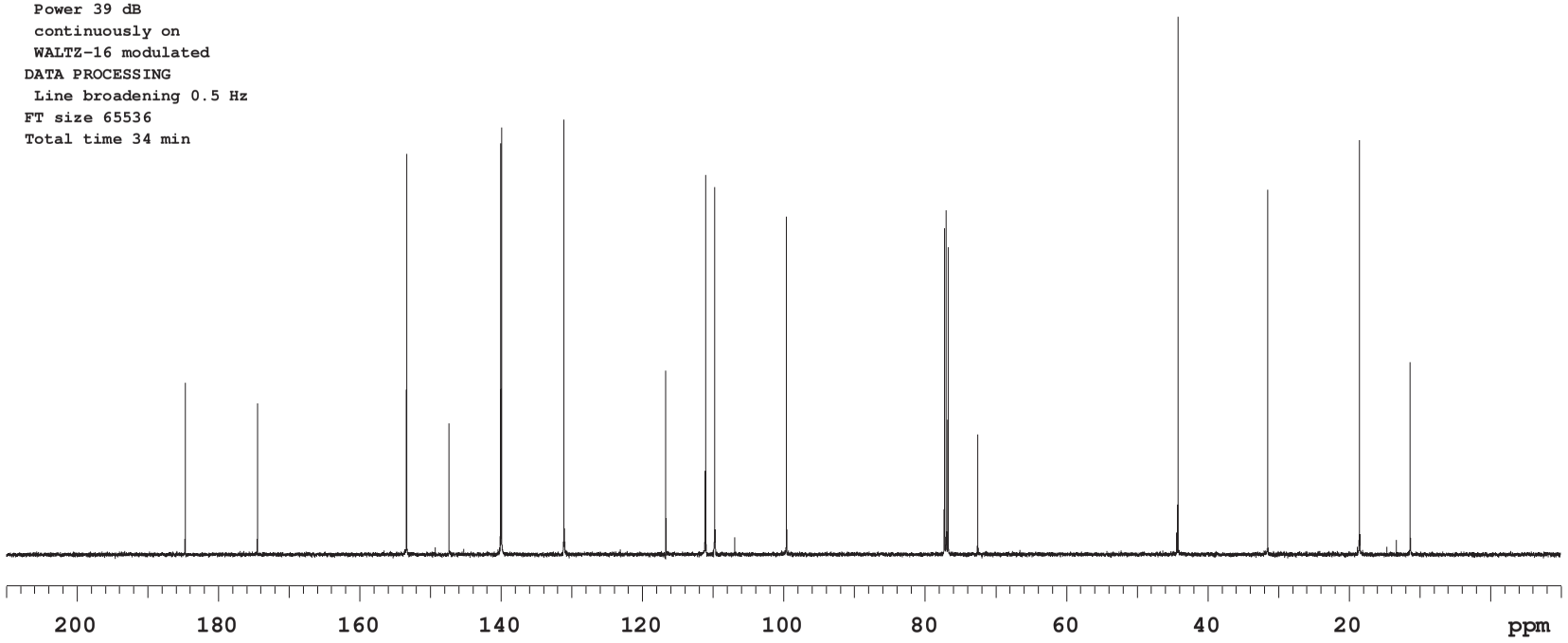
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 3 2011

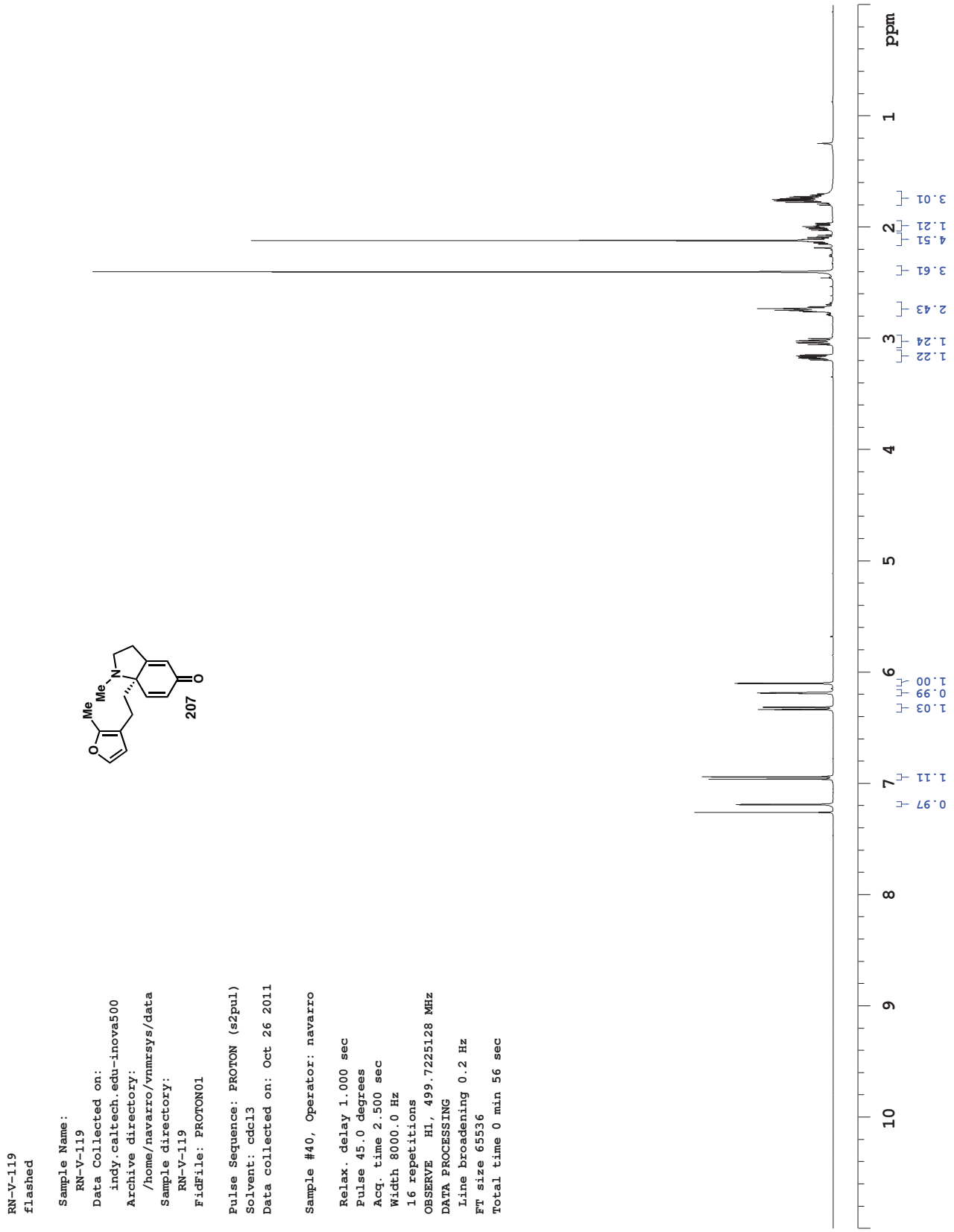
Sample #40, Operator: navarro

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6553348 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min



S18




RN-V-119
flashed
Sample Name:
RN-V-119
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-119
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 26 2011
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7225128 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 56 sec
Me
Me
N
O
O
207
ppm
10
9
8
7
6
5
4
3
2
1
0.97
1.11
1.00
0.99
1.03
1.22
1.24
2.43
3.61
4.51
1.21
3.01

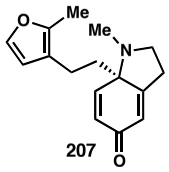
RN-V-119
flashed

Sample Name:
RN-V-119
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-119
FidFile: CARBON01

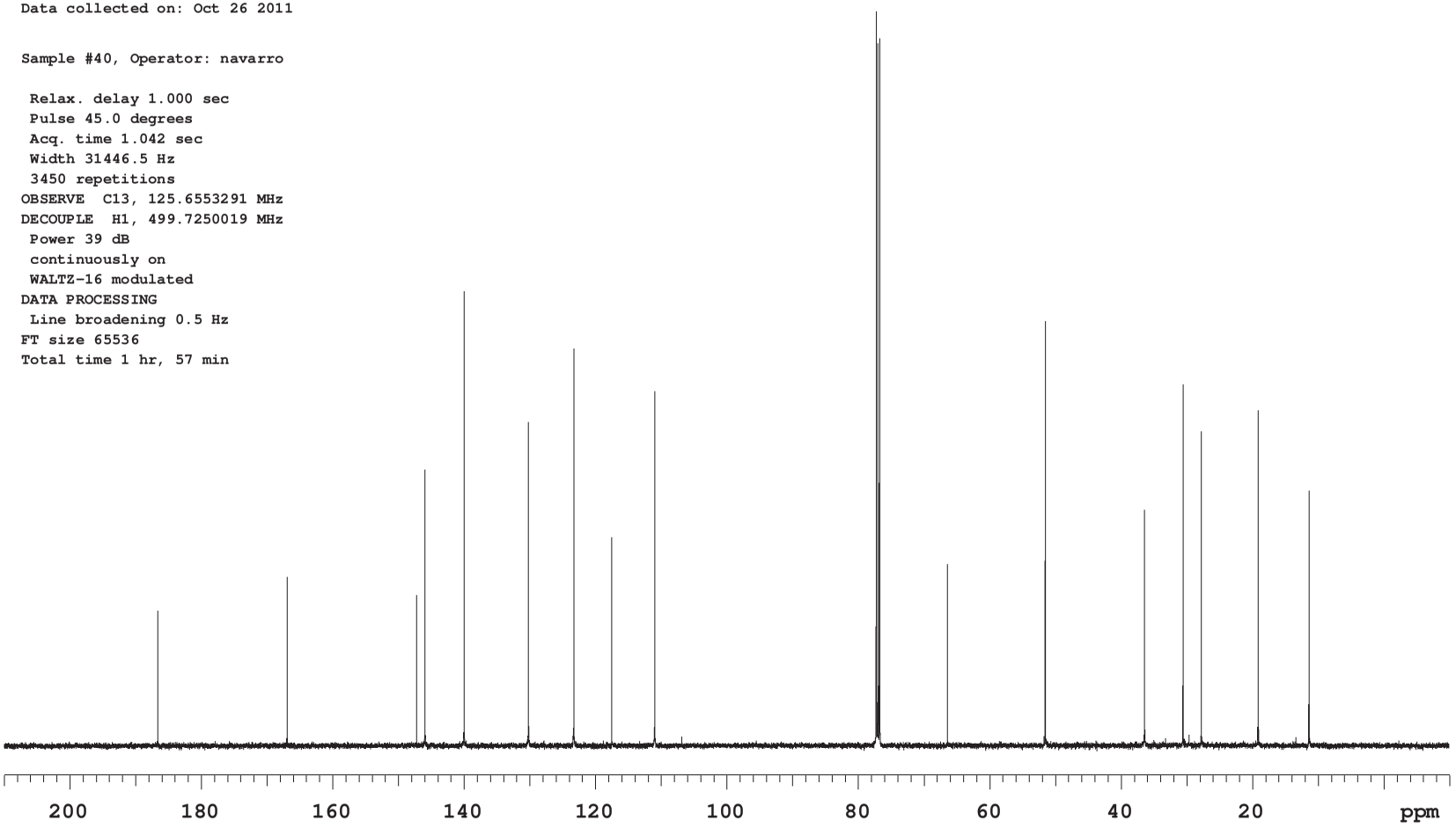
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 26 2011

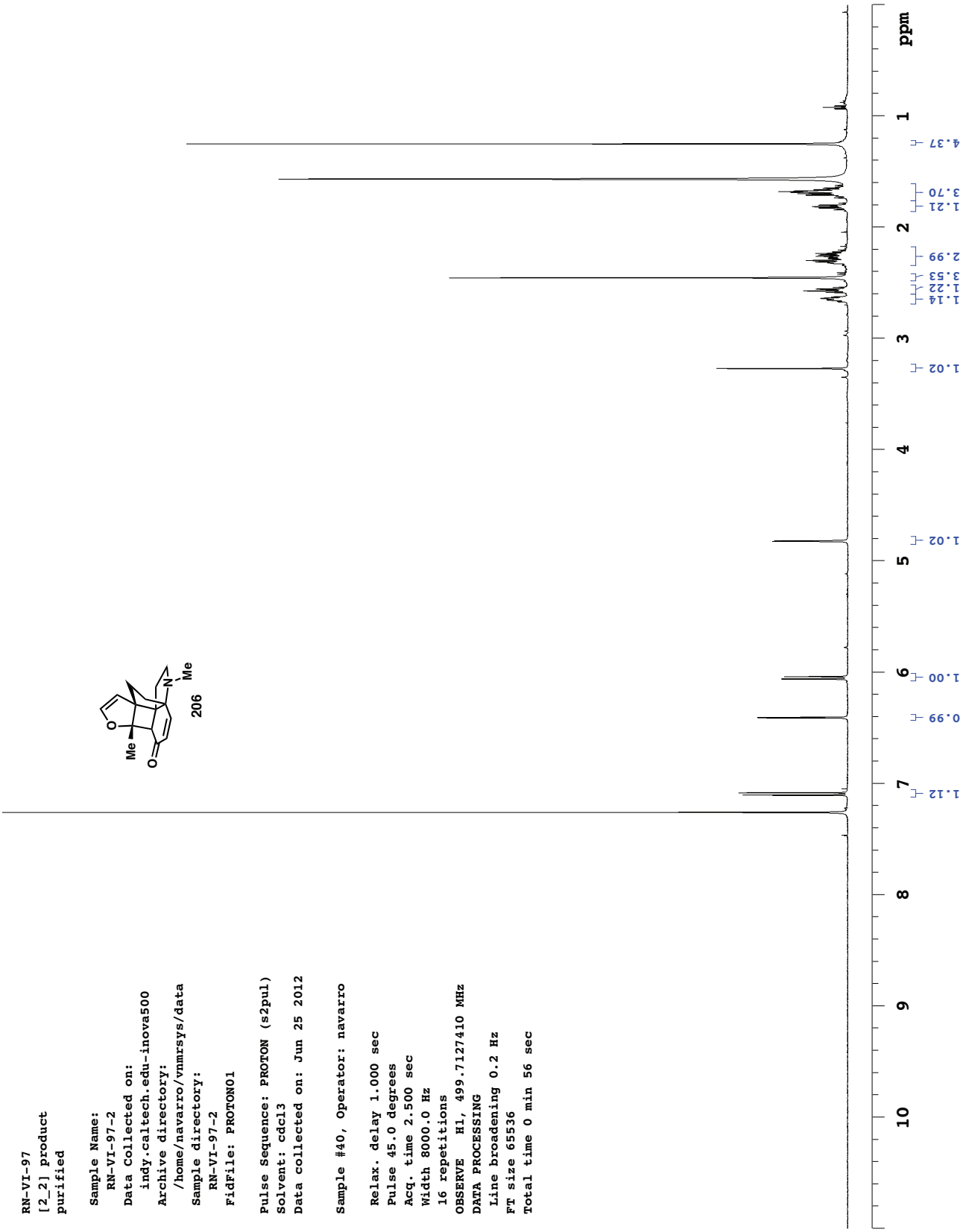
Sample #40, Operator: navarro

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
3450 repetitions
OBSERVE C13, 125.6553291 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 57 min



207




RN-VI-97
[2_2] product
purified
Sample Name:
RN-VI-97-2
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-97-2
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 25 2012
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7127410 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 56 sec
206
Me
N
Me
O
O
ppm
1
2
3
4
5
6
7
8
9
10
4.37
3.70
1.21
2.99
3.53
1.22
1.14
1.02
1.02
1.00
0.99
1.12

Std proton

Sample Name:

Data Collected on:
daytona.caltech.edu-inova500
Archive directory:

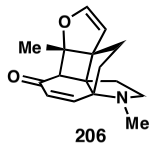
Sample directory:

FidFile: RN-VI-97-2_13C

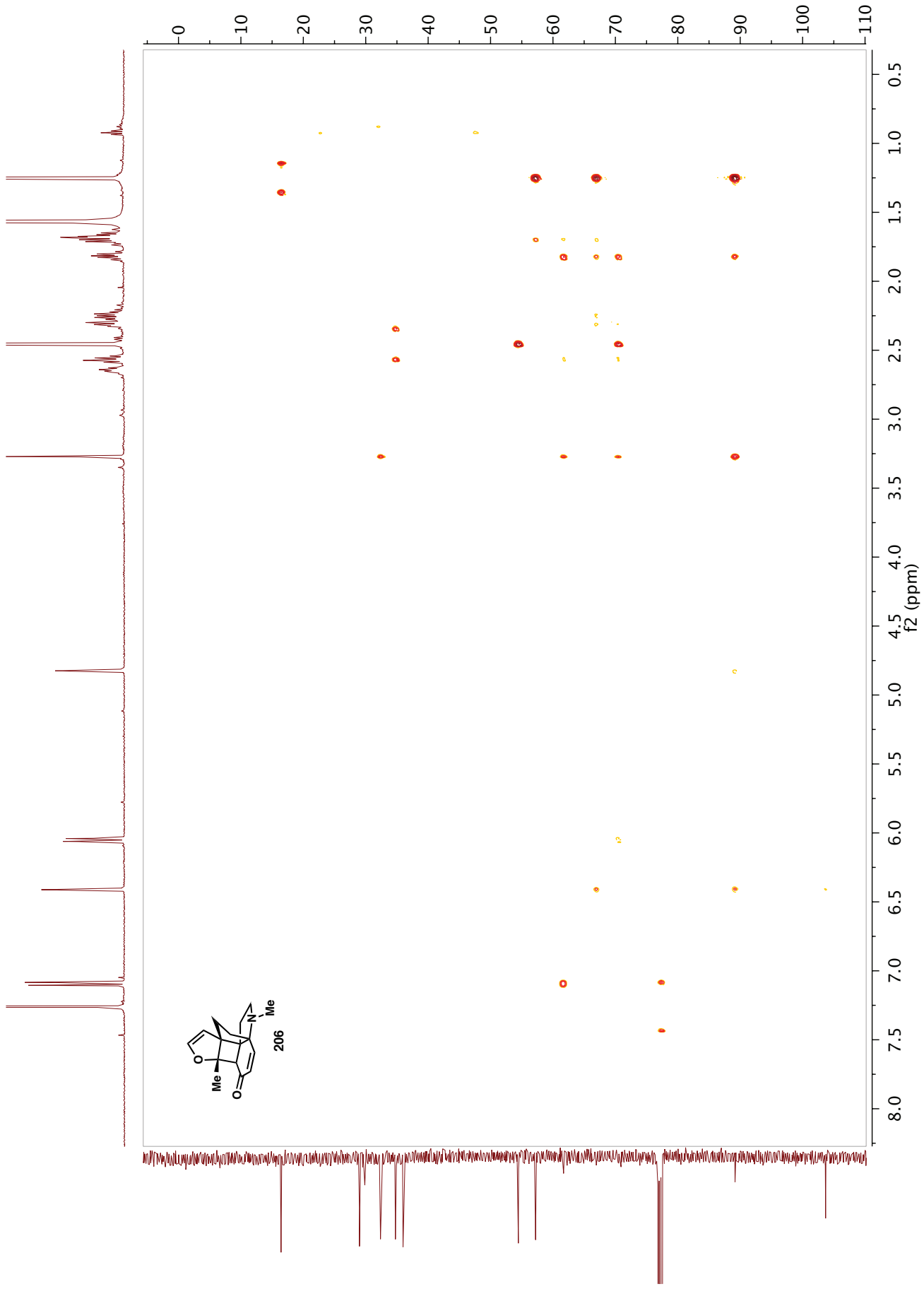
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 28 2012

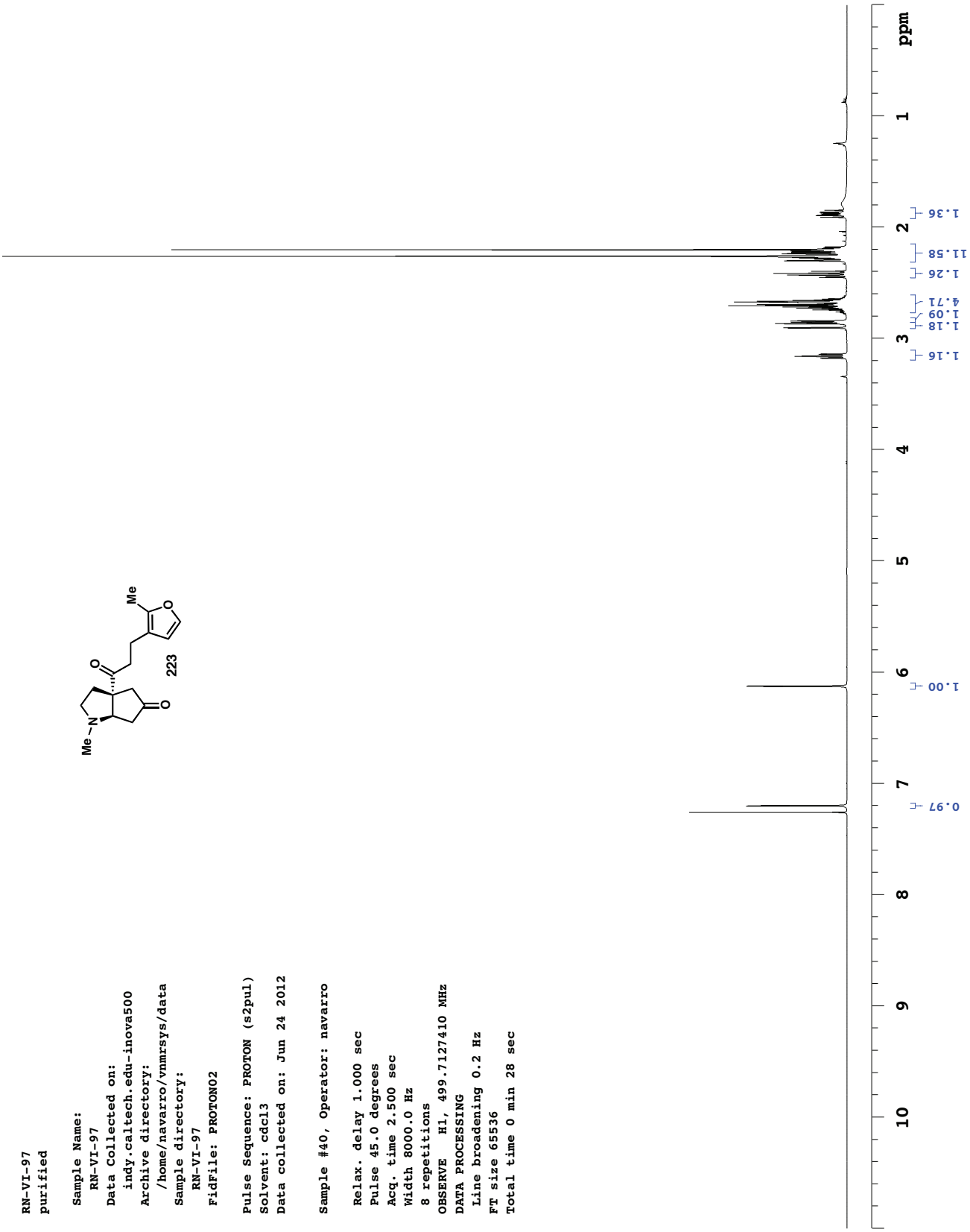
Temp. 25.0 C / 298.1 K
Operator: navarro

Relax. delay 0.800 sec
Pulse 45.0 degrees
Acq. time 1.043 sec
Width 31421.8 Hz
8736 repetitions
OBSERVE C13, 125.6871026 MHz
DECOUPLE H1, 499.8513810 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
Total time 5 hr, 33 min



206


f1 (ppm)
0
10
20
30
40
50
60
70
80
90
100
110
f2 (ppm)
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
Me
N
Me
O
O
Me
206


RN-VI-97
purified
Sample Name:
RN-VI-97
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-97
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 24 2012
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7127410 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 28 sec
Me
O
O
O
Me
N
223
ppm
1
2
3
4
5
6
7
8
9
10
1.36
11.58
1.26
4.71
1.09
1.18
1.16
1.00
0.97

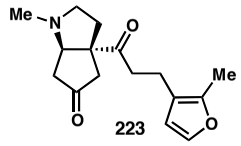
RN-VI-97
purified

Sample Name:
RN-VI-97
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-97
FidFile: CARBON01

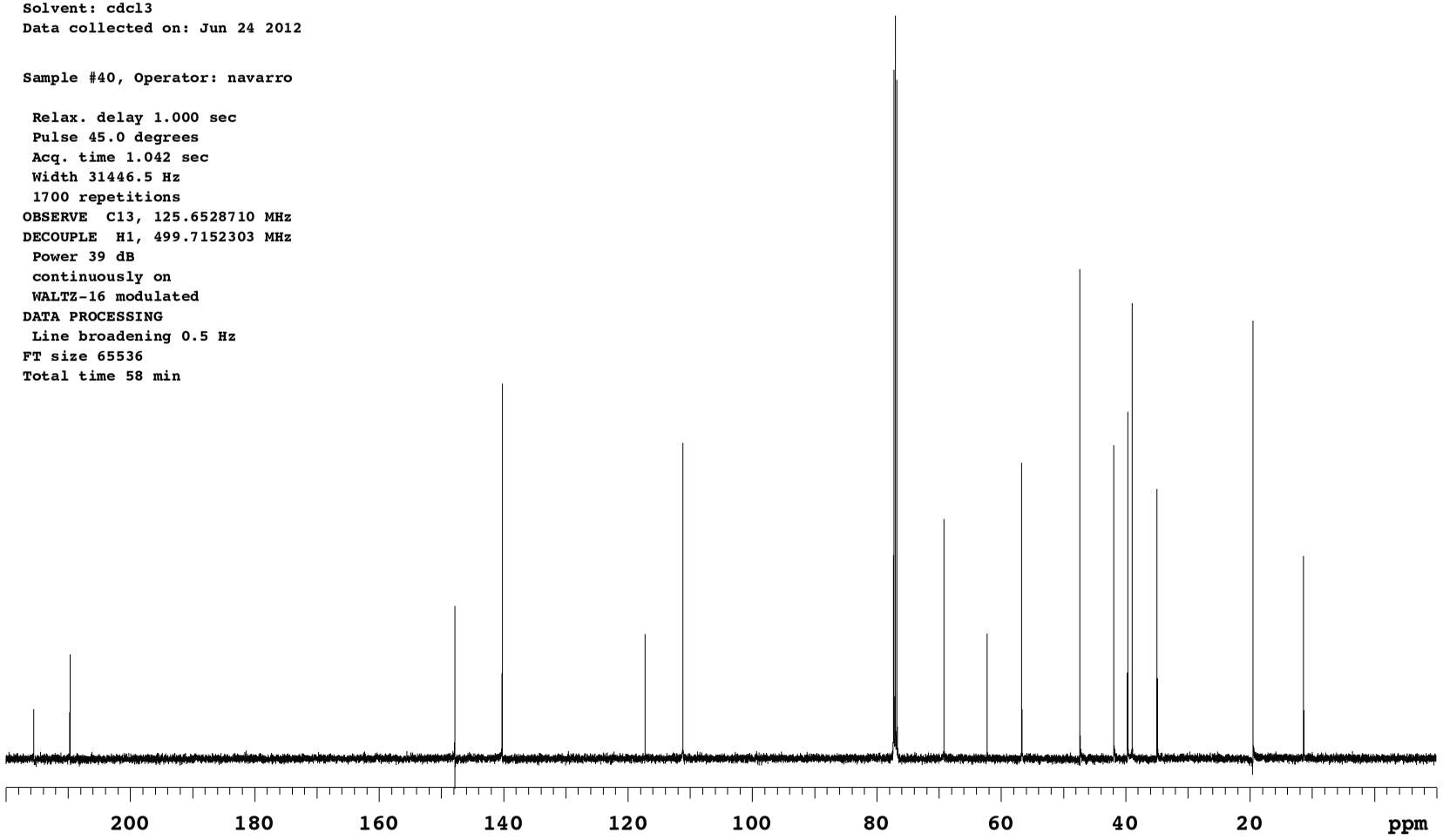
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 24 2012

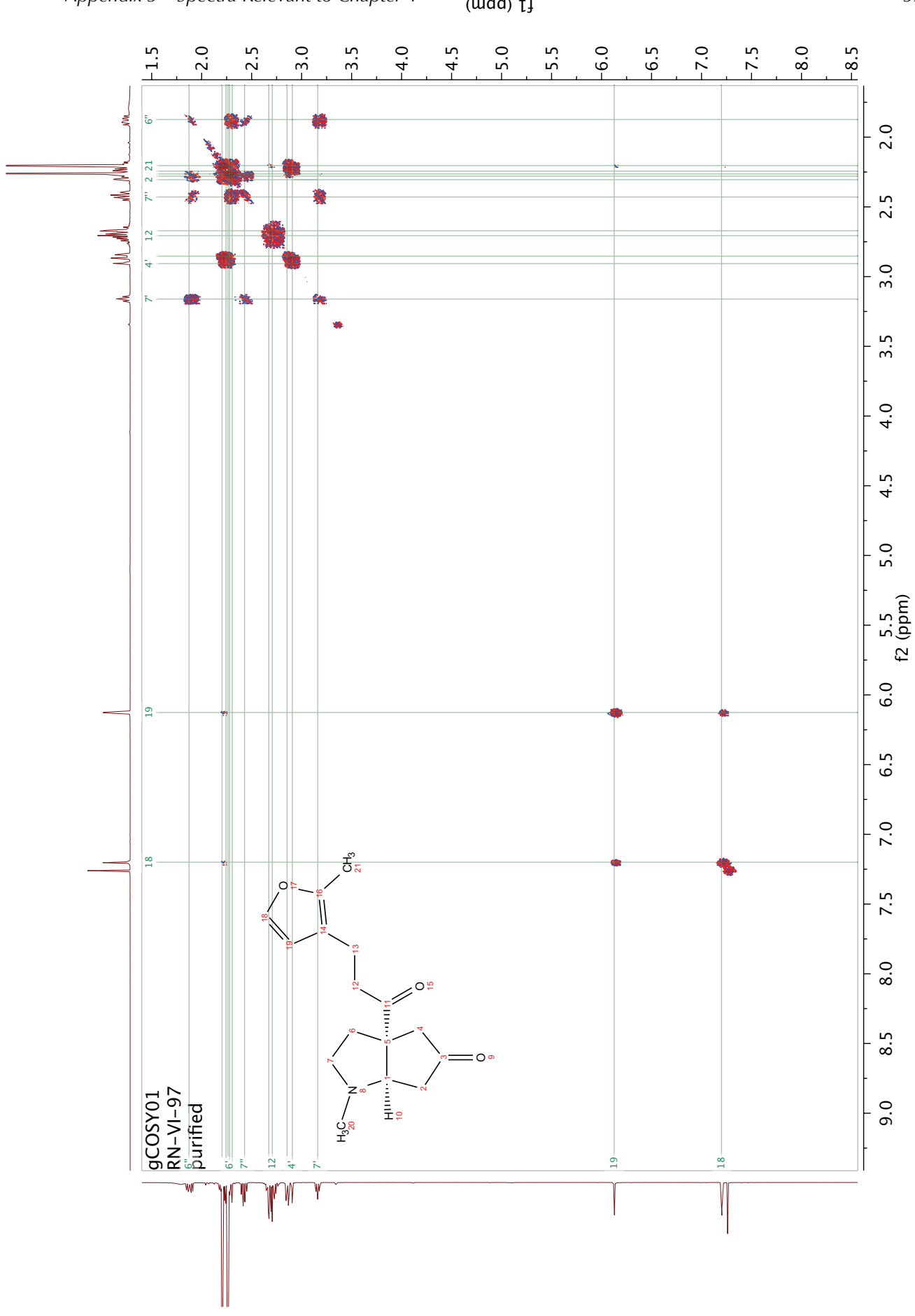
Sample #40, Operator: navarro

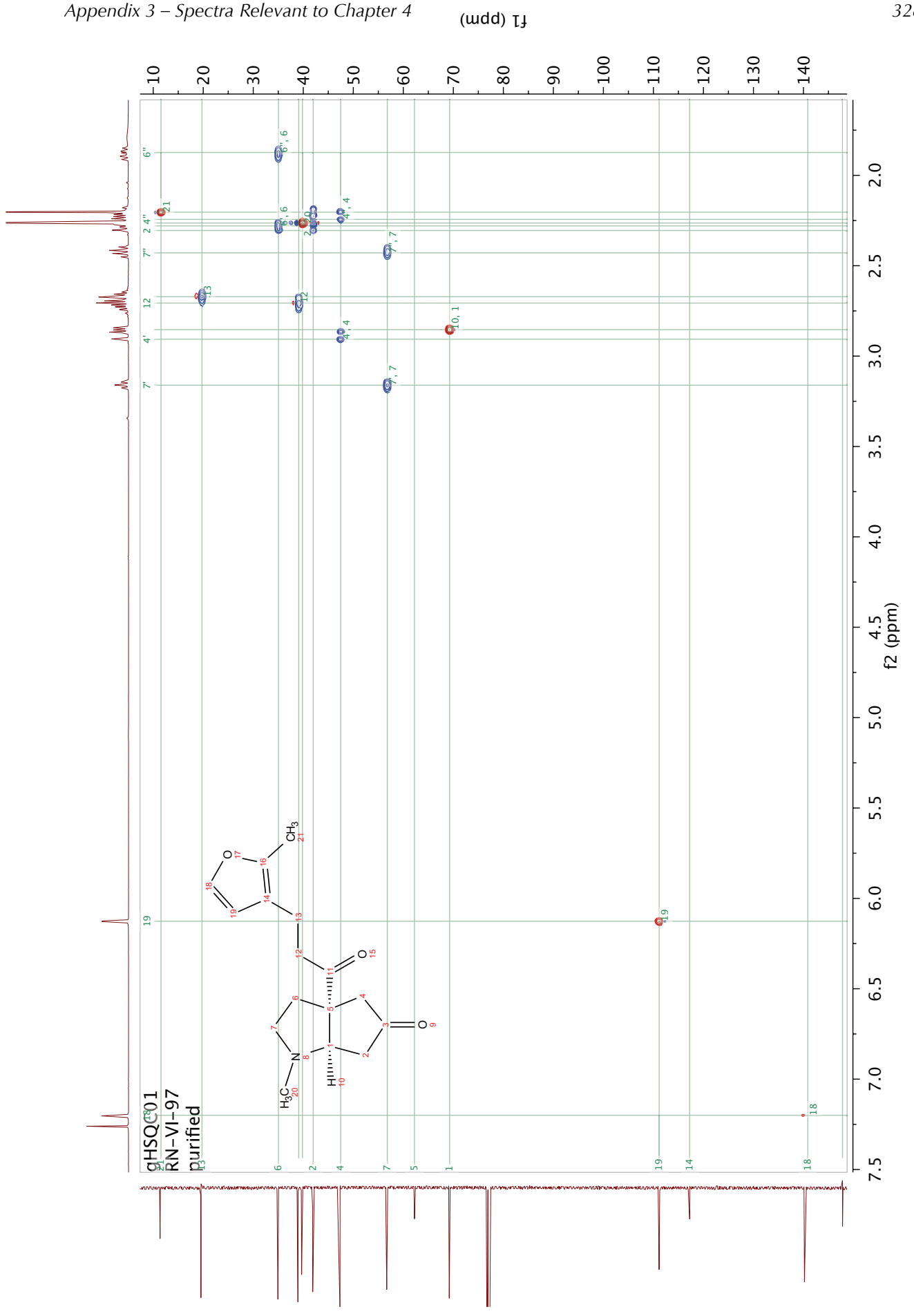
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1700 repetitions
OBSERVE C13, 125.6528710 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 58 min

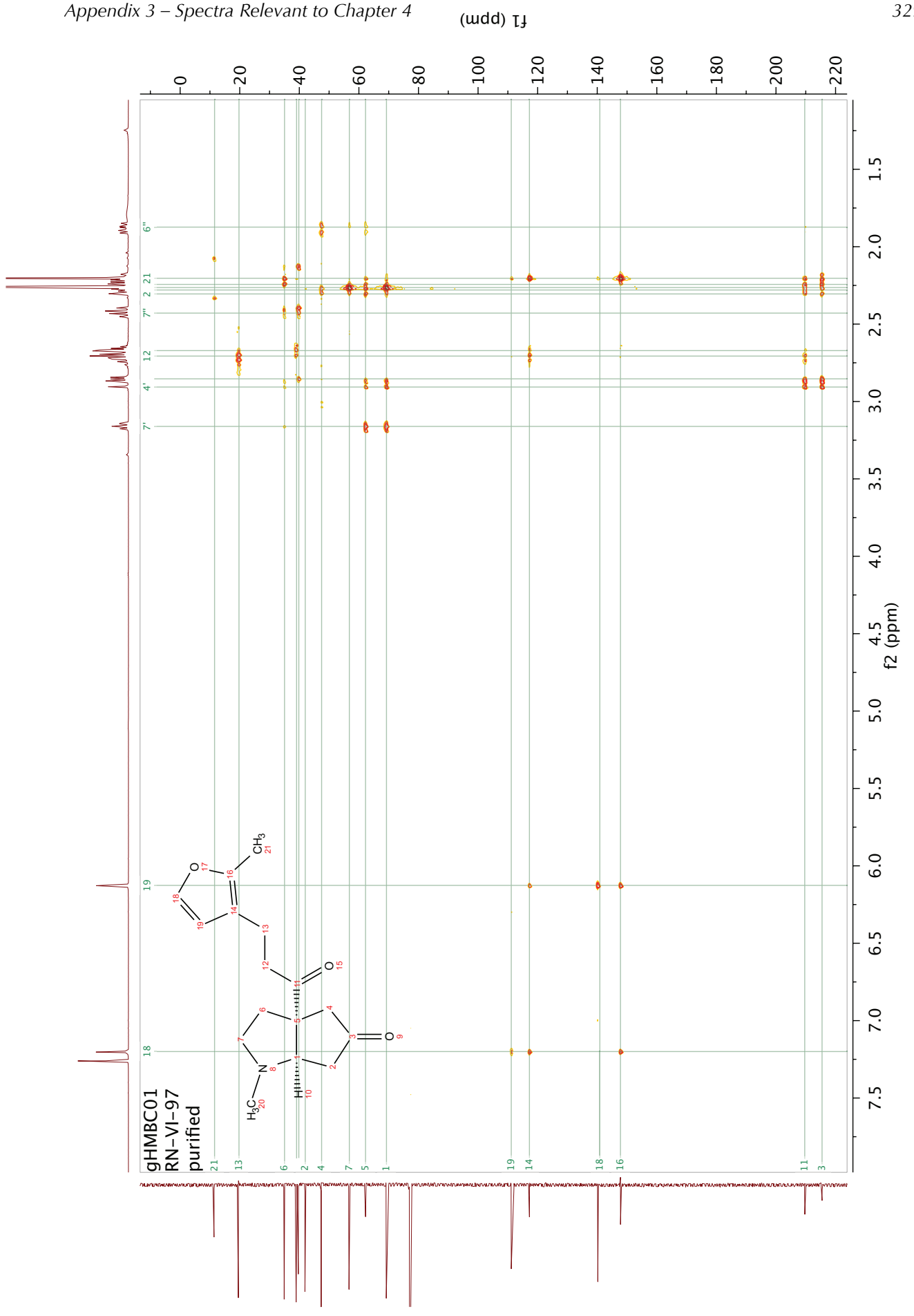


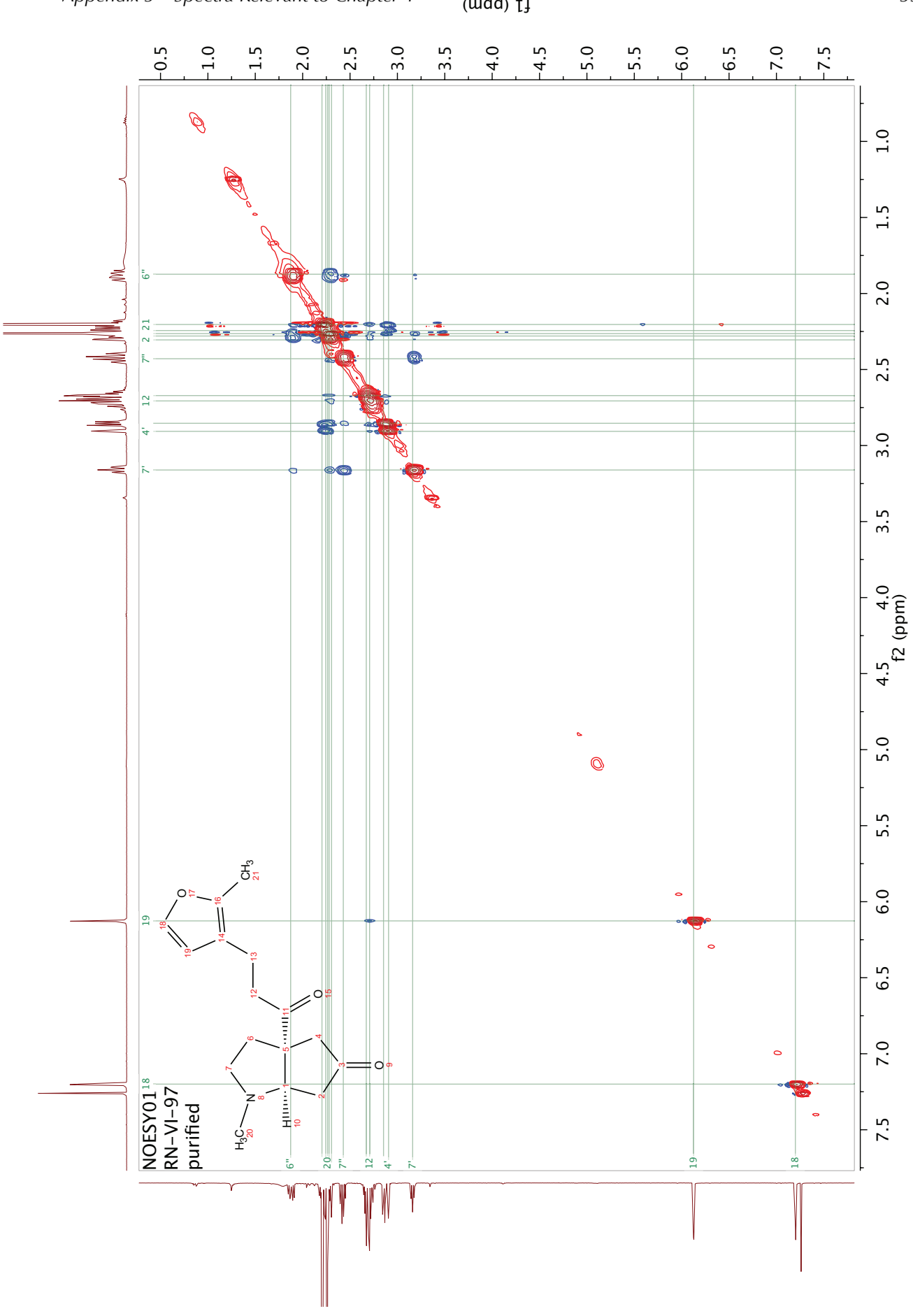
223

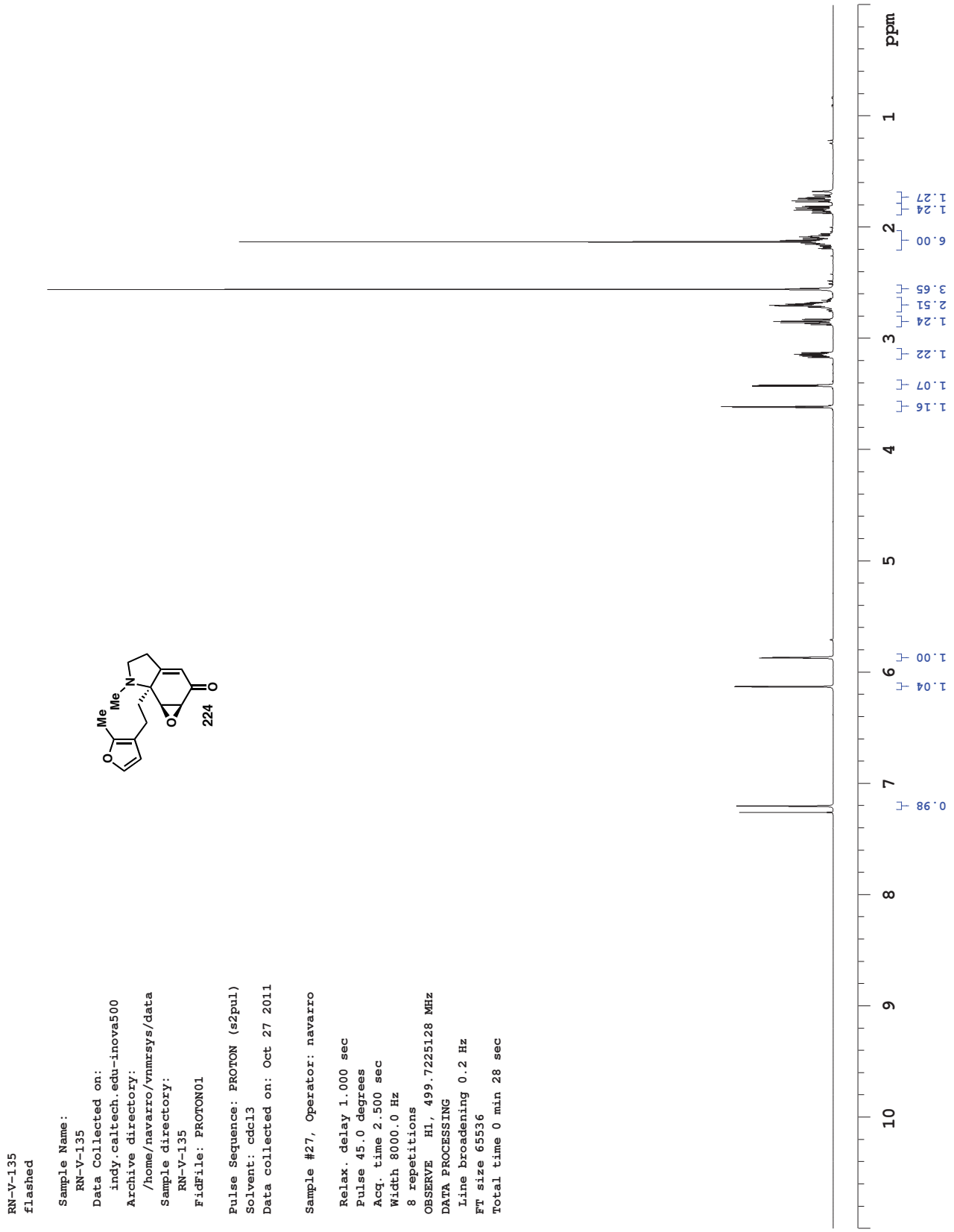



gCOSY01
RN-VI-97
purified
f1 (ppm)
f2 (ppm)


f1 (ppm)
f2 (ppm)
gHSQC01
RN-VI-97
purified


gHMBC01
RN-VI-97
purified
f1 (ppm)
f2 (ppm)


NOESY01
RN-VI-97
purified
f2 (ppm)
f1 (ppm)


RN-V-135
flashed
Sample Name:
RN-V-135
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-135
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 27 2011
Sample #27, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7225128 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 28 sec
Me
Me
N
O
O
224
O
ppm
1
2
3
4
5
6
7
8
9
10
1.27
1.24
6.00
3.65
2.51
1.24
1.22
1.07
1.16
1.00
1.04
0.98

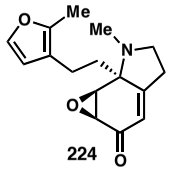
RN-V-135
flashed

Sample Name:
RN-V-135
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-135
FidFile: CARBON01

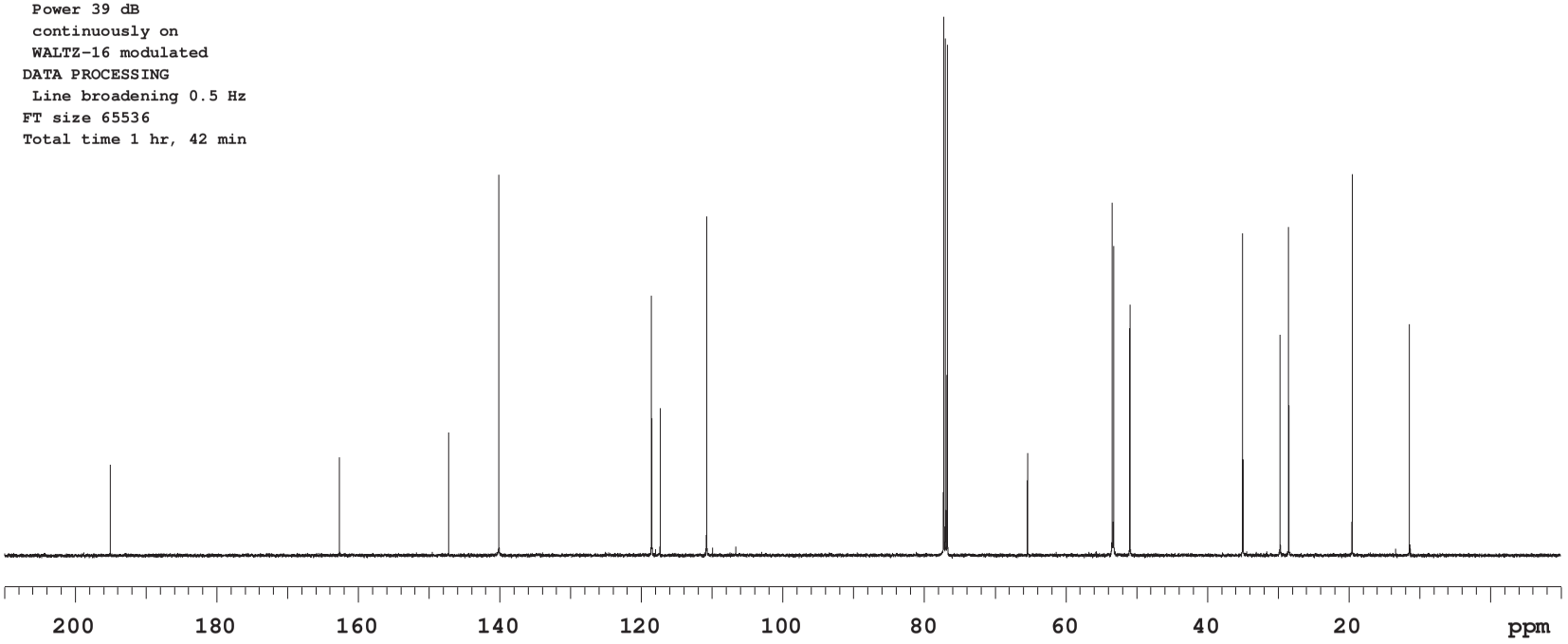
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 27 2011

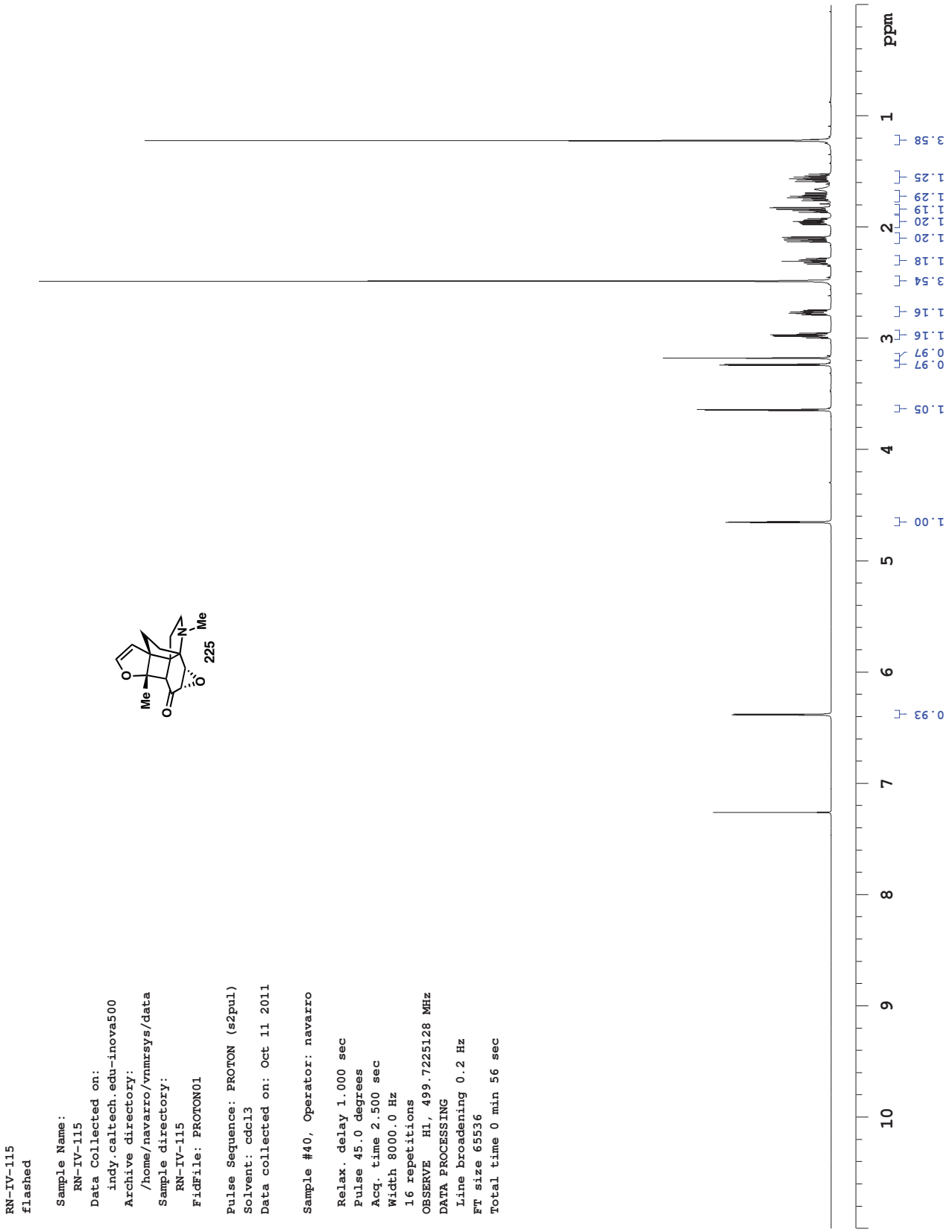
Sample #27, Operator: navarro

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
3000 repetitions
OBSERVE C13, 125.6553300 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 42 min



224




RN-IV-115
flashed
Sample Name:
RN-IV-115
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-IV-115
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 11 2011
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7225128 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 56 sec
Me
N
Me
O
O
O
225
ppm
10
9
8
7
6
5
4
3
2
1
0.93
1.00
1.05
0.97
0.97
1.16
1.16
1.54
1.18
1.20
1.20
1.19
1.29
1.25
3.58

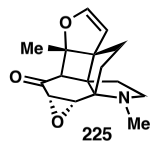
RN-IV-115
flashed

Sample Name:
RN-IV-115
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-IV-115
FidFile: CARBON01

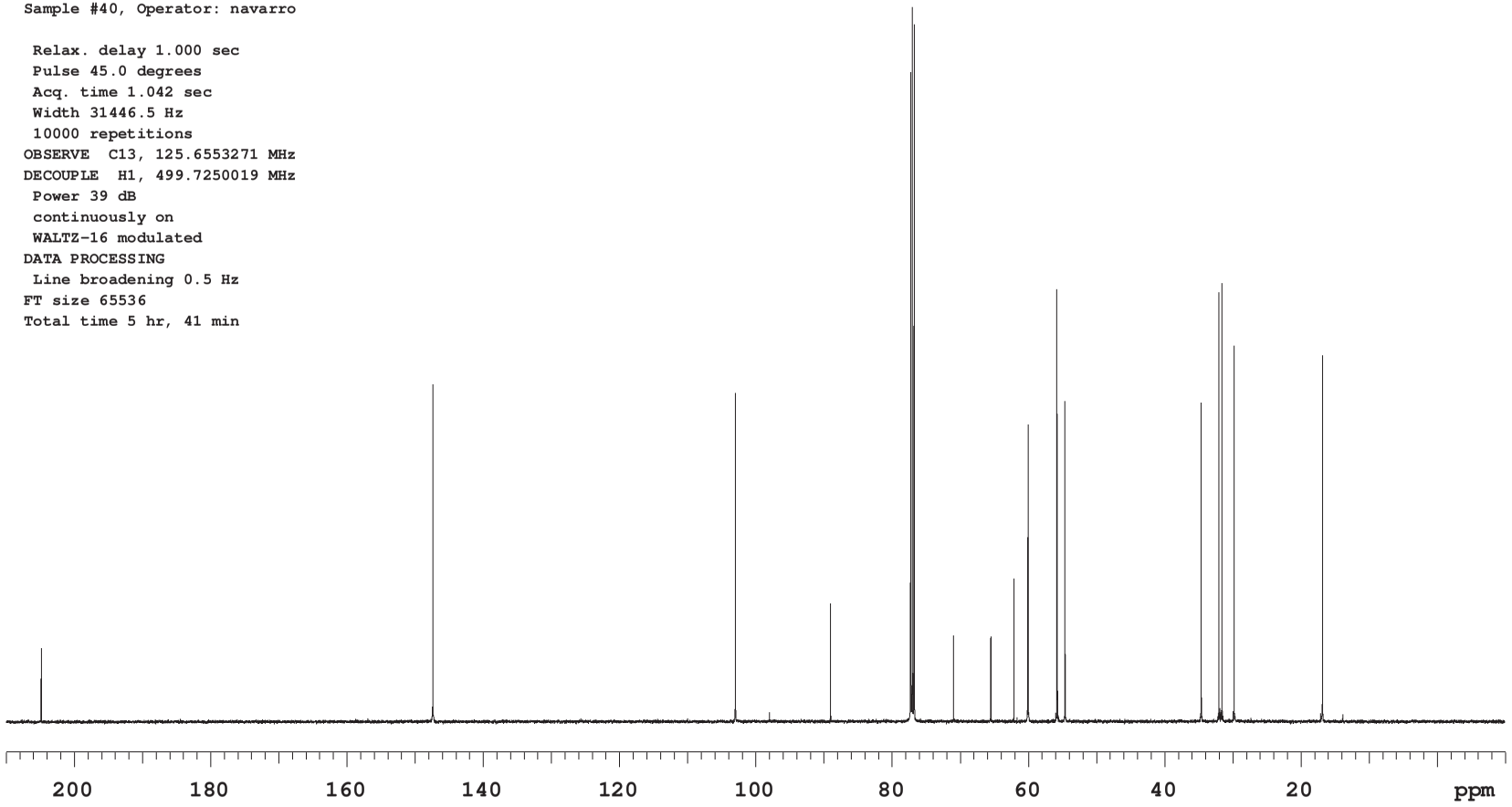
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 11 2011

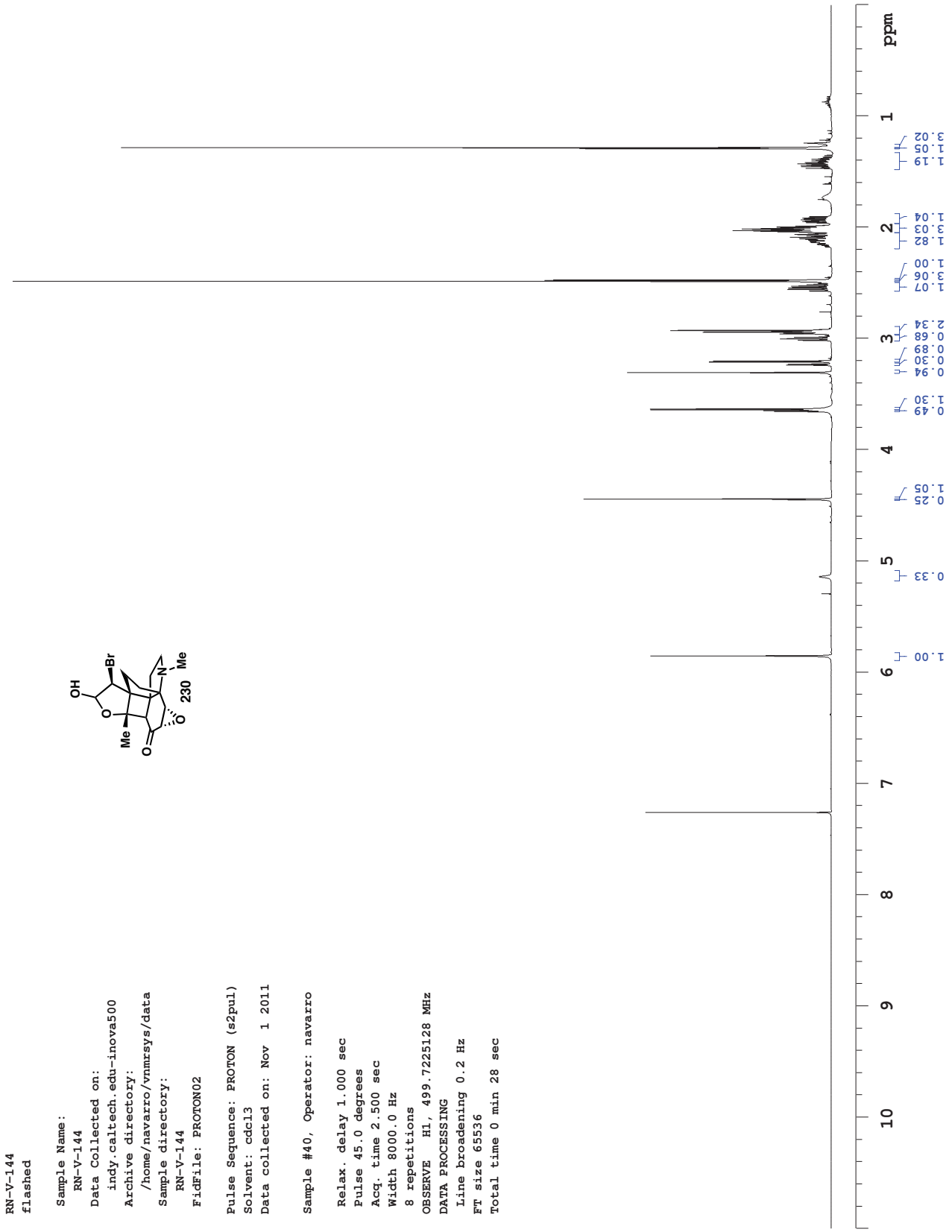
Sample #40, Operator: navarro

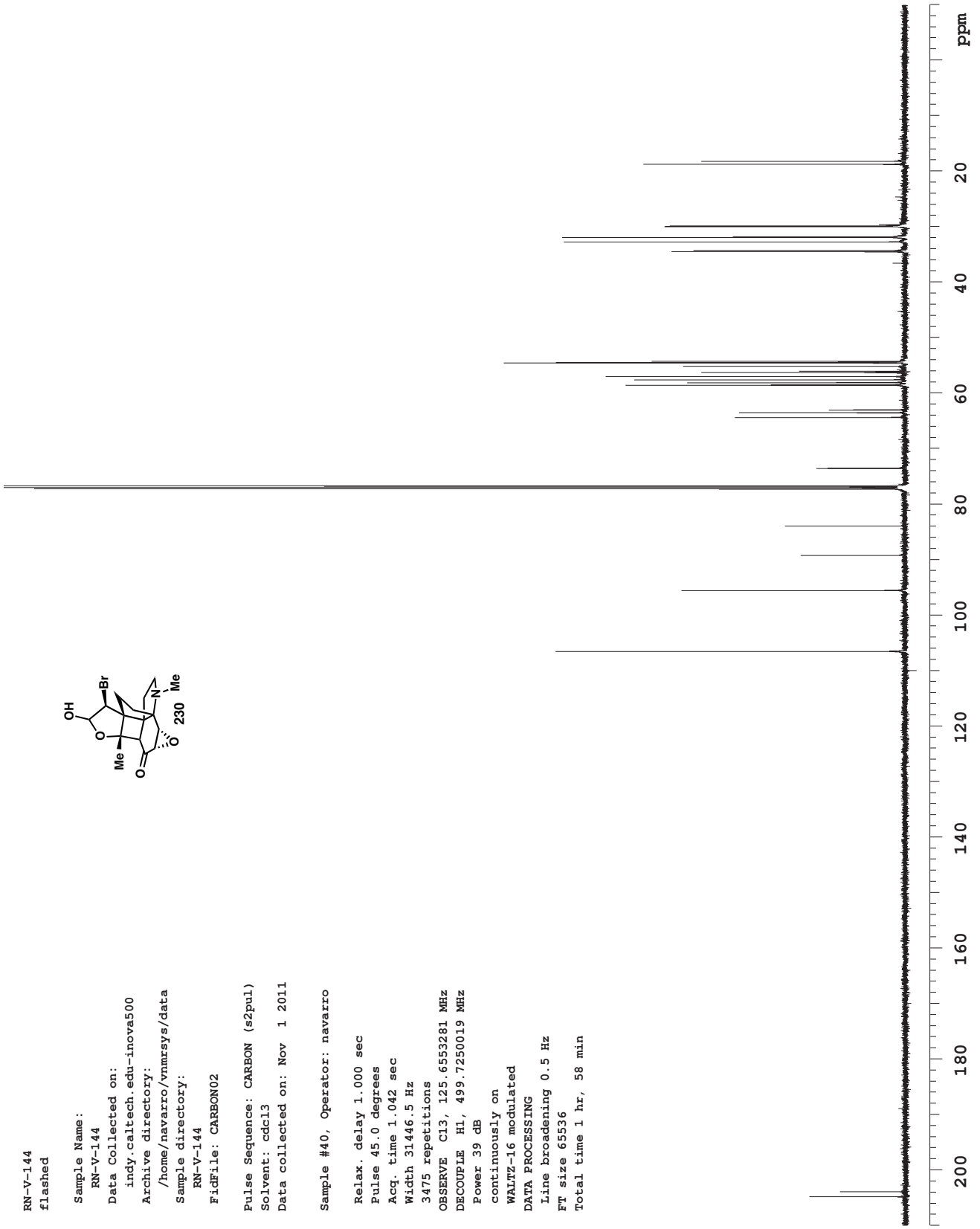
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
10000 repetitions
OBSERVE C13, 125.6553271 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 5 hr, 41 min

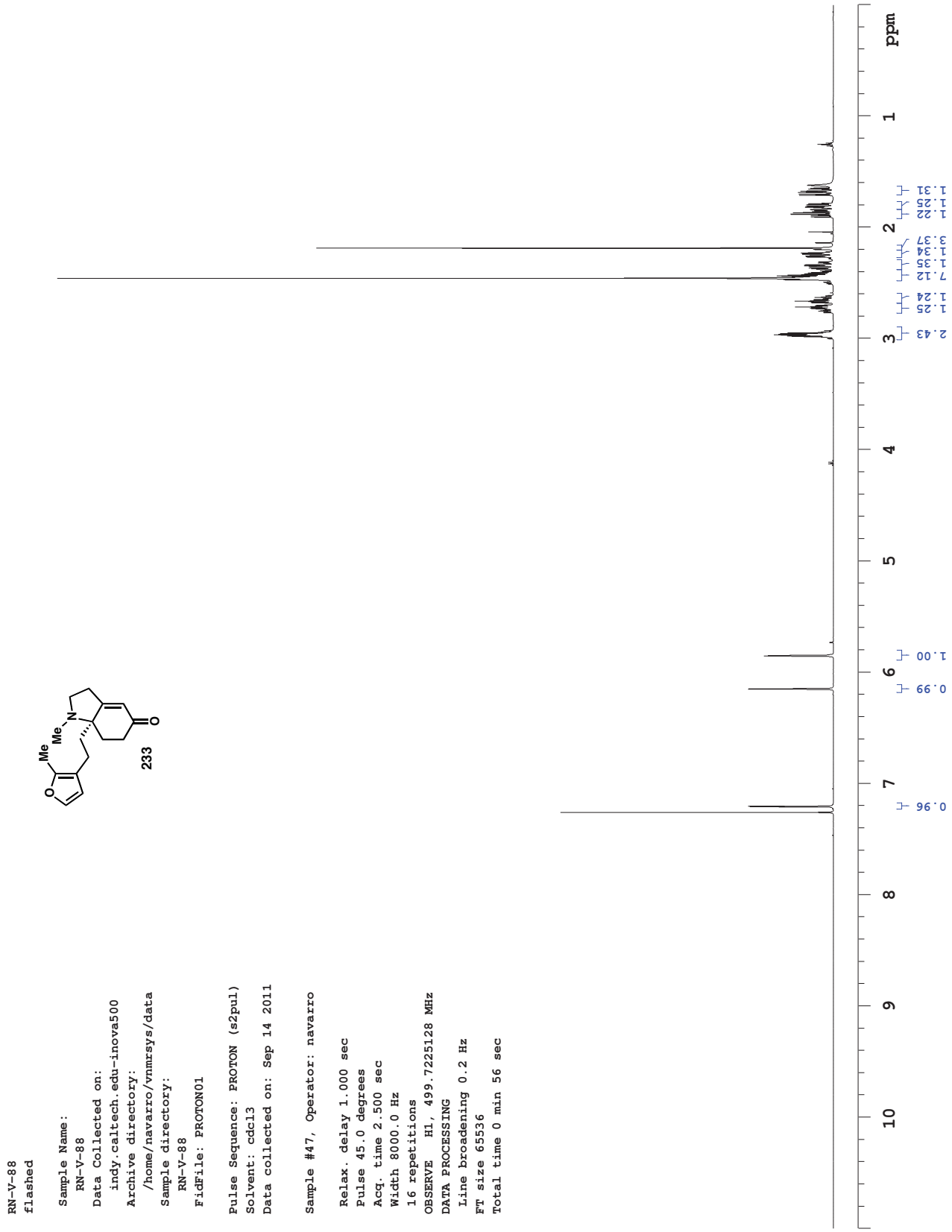


225




RN-V-144
flashed
Sample Name:
RN-V-144
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-144
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Nov 1 2011
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7225128 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 28 sec
OH
Br
N
Me
O
Me
O
230
O
ppm
1
2
3
4
5
6
7
8
9
10
3.02
1.05
1.19
1.04
3.03
1.82
1.00
3.06
1.07
2.34
0.68
0.89
0.30
0.94
1.30
0.49
1.05
0.25
0.33
1.00


RN-V-144
flashed
Sample Name:
RN-V-144
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-144
FidFile: CARBON02
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Nov 1 2011
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
3475 repetitions
OBSERVE C13, 125.6553281 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 58 min
OH
Br
N
Me
O
Me
O
O
230
200
180
160
140
120
100
80
60
40
20
ppm


RN-V-88
flashed
Sample Name:
RN-V-88
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-88
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 14 2011
Sample #47, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7225128 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 56 sec
Me
Me
N
O
O
233
ppm
1
2
3
4
5
6
7
8
9
10
1.00
0.99
0.96
1.31
1.25
1.22
3.37
1.34
1.35
7.12
1.24
1.25
2.43

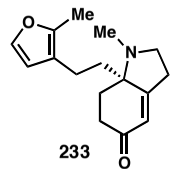
RN-V-88
flashed

Sample Name:
RN-V-88
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-88
FidFile: CARBON01

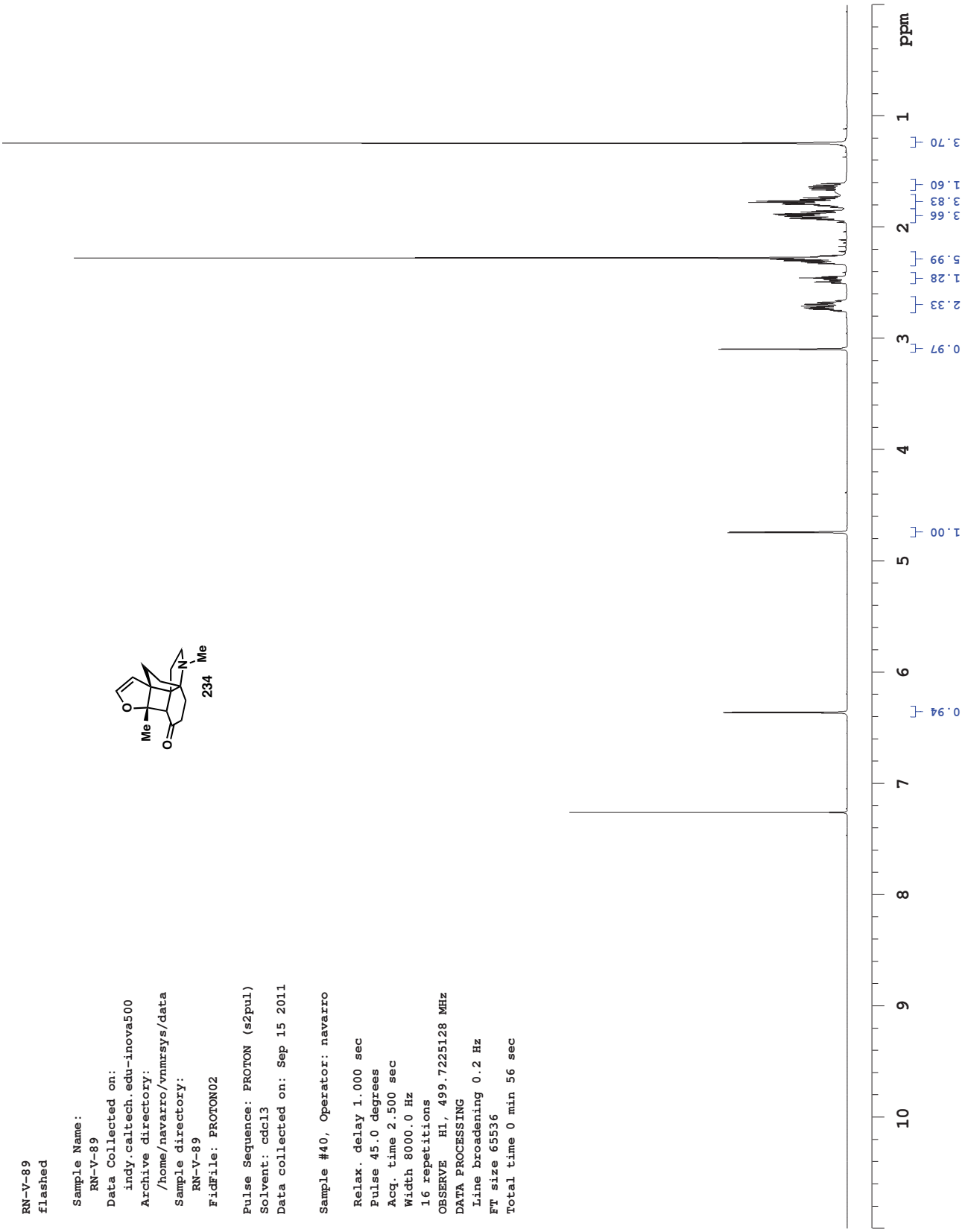
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 14 2011

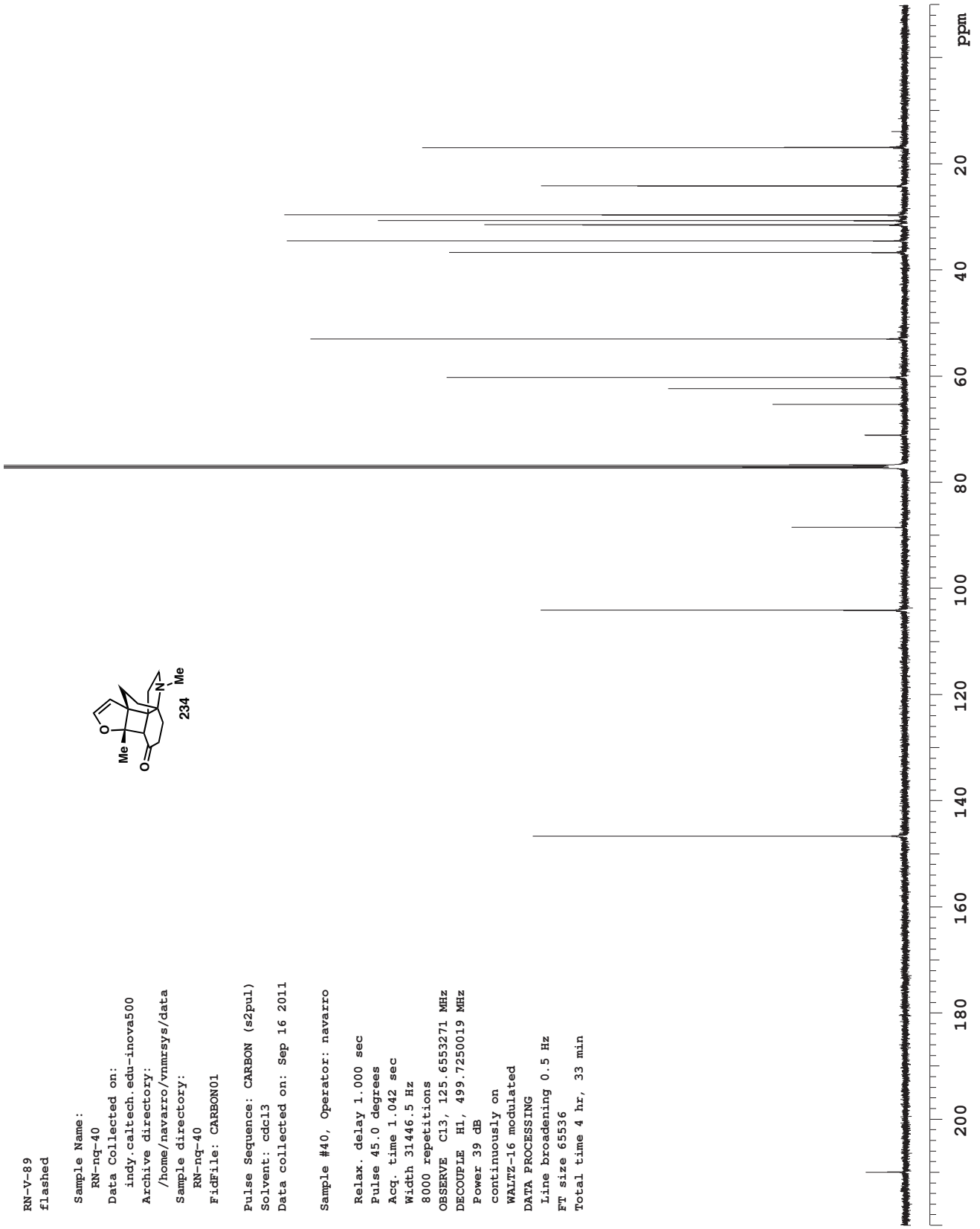
Sample #47, Operator: navarro

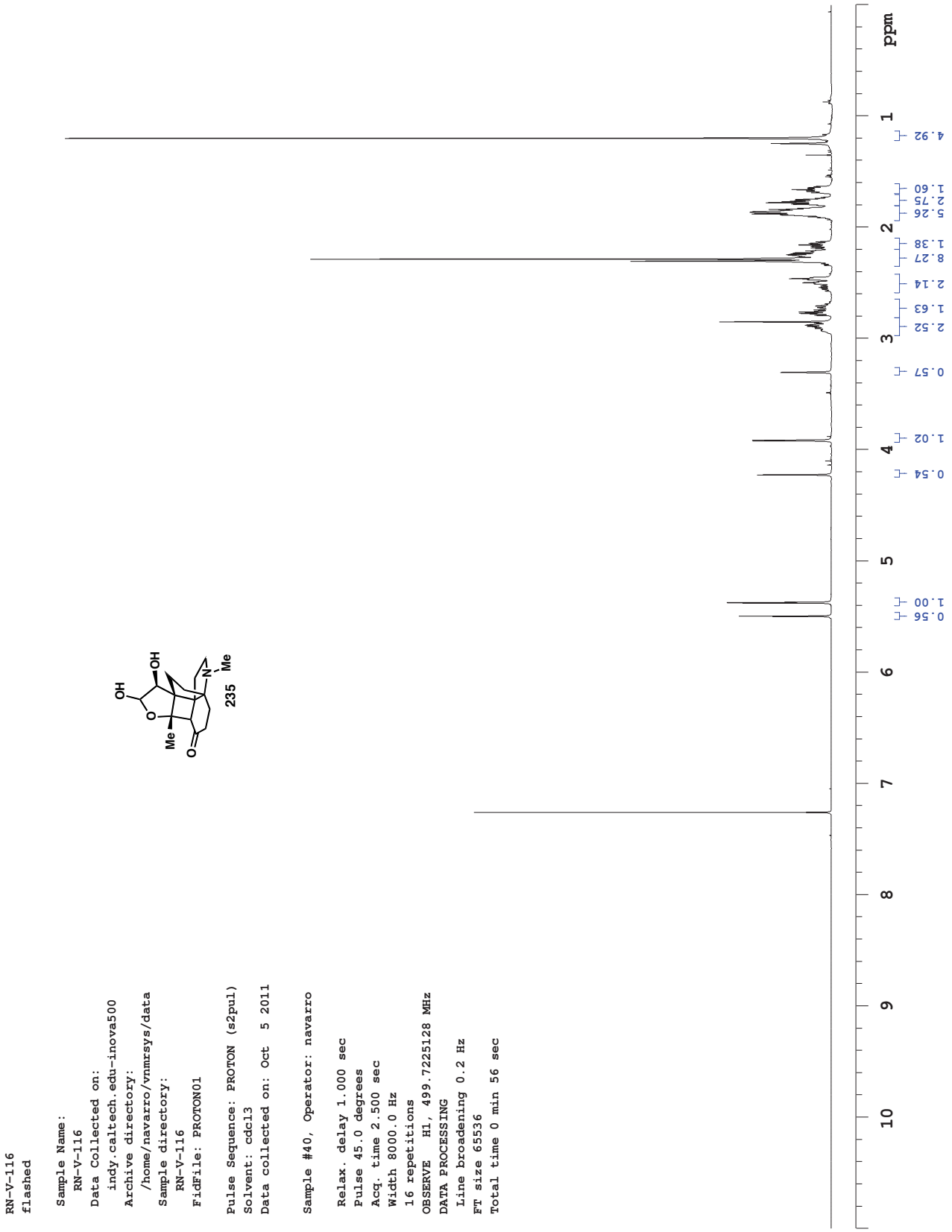
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6553271 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min



233


RN-V-89
flashed
Sample Name:
RN-V-89
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-89
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 15 2011
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7225128 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 56 sec
Me
O
Me
N
234
ppm
10
9
8
7
6
5
4
3
2
1
0.94
1.00
0.97
2.33
1.28
5.99
3.66
3.83
1.60
3.70


RN-V-89
flashed
Sample Name:
RN-nq-40
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-nq-40
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 16 2011
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
8000 repetitions
OBSERVE C13, 125.6553271 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 4 hr, 33 min
Me
O
Me
N
234
200
180
160
140
120
100
80
60
40
20
ppm


RN-V-116
flashed
Sample Name:
RN-V-116
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-116
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 5 2011
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7225128 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 56 sec
OH
OH
O
Me
O
N
Me
235
ppm
10
9
8
7
6
5
4
3
2
1
4.92
1.60
2.75
5.26
1.38
8.27
2.14
1.63
2.52
0.57
1.02
0.54
1.00
0.56

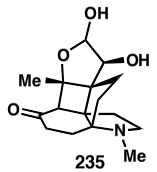
RN-V-116
flashed

Sample Name:
RN-V-116
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-116
FidFile: CARBON02

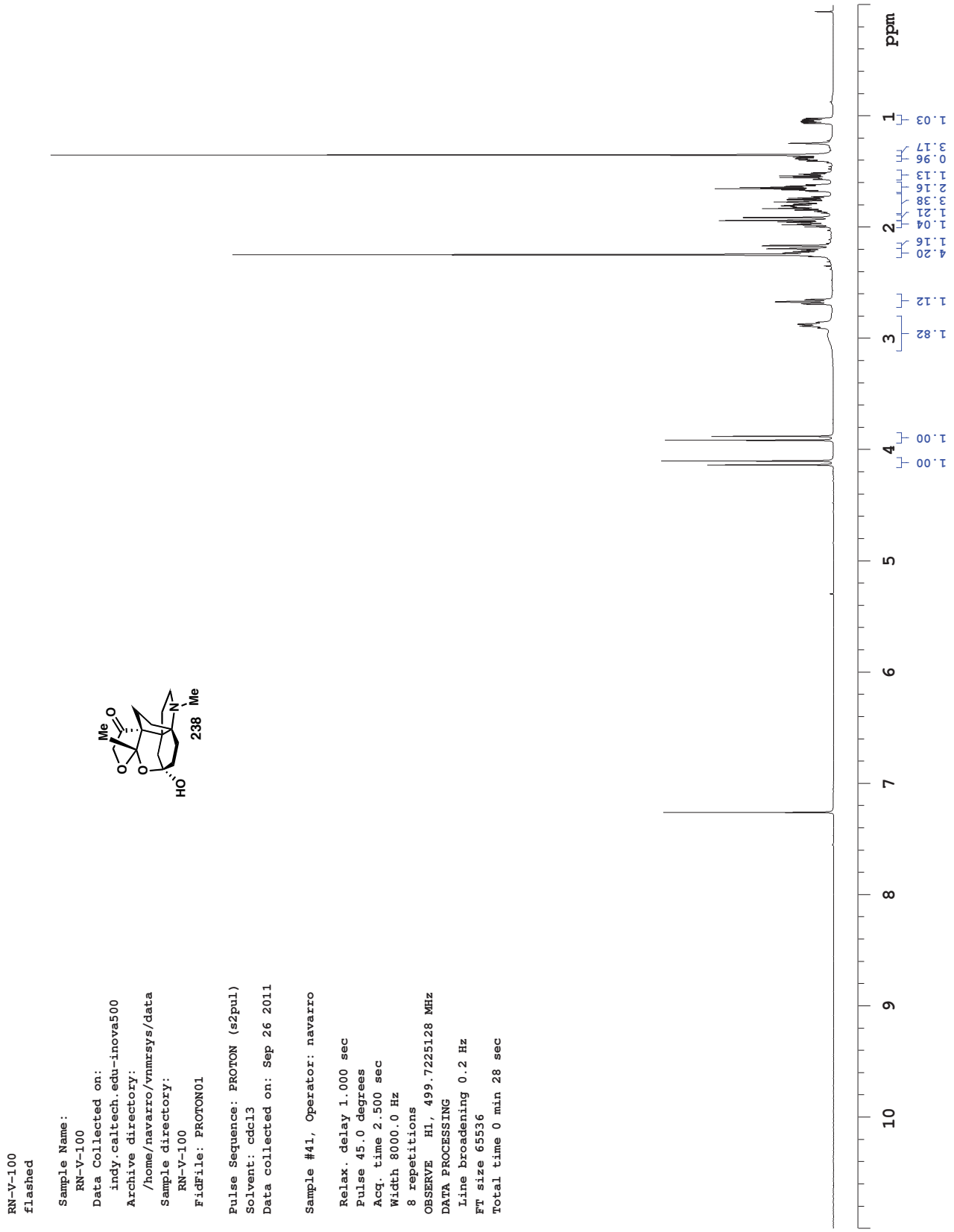
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 5 2011

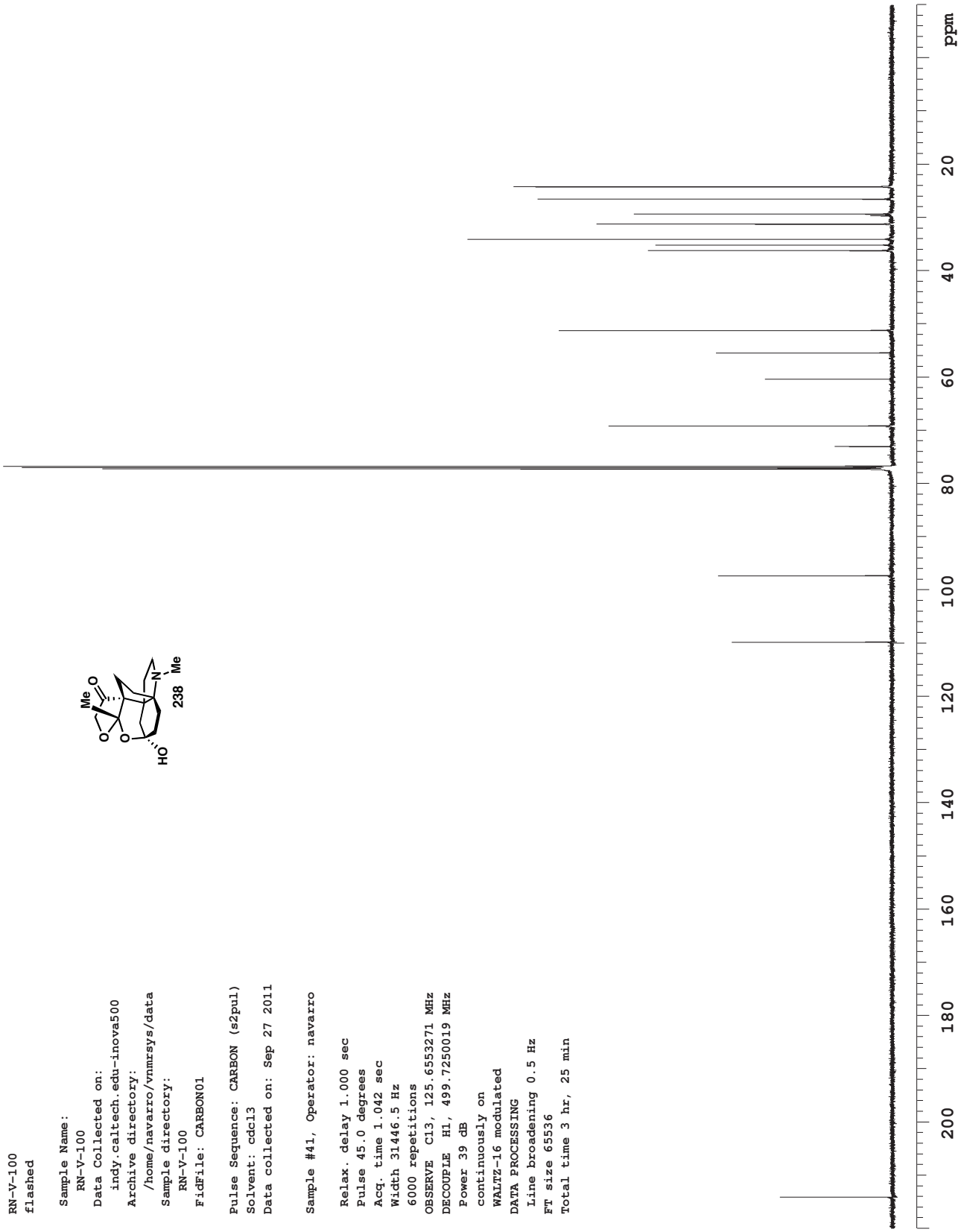
Sample #40, Operator: navarro

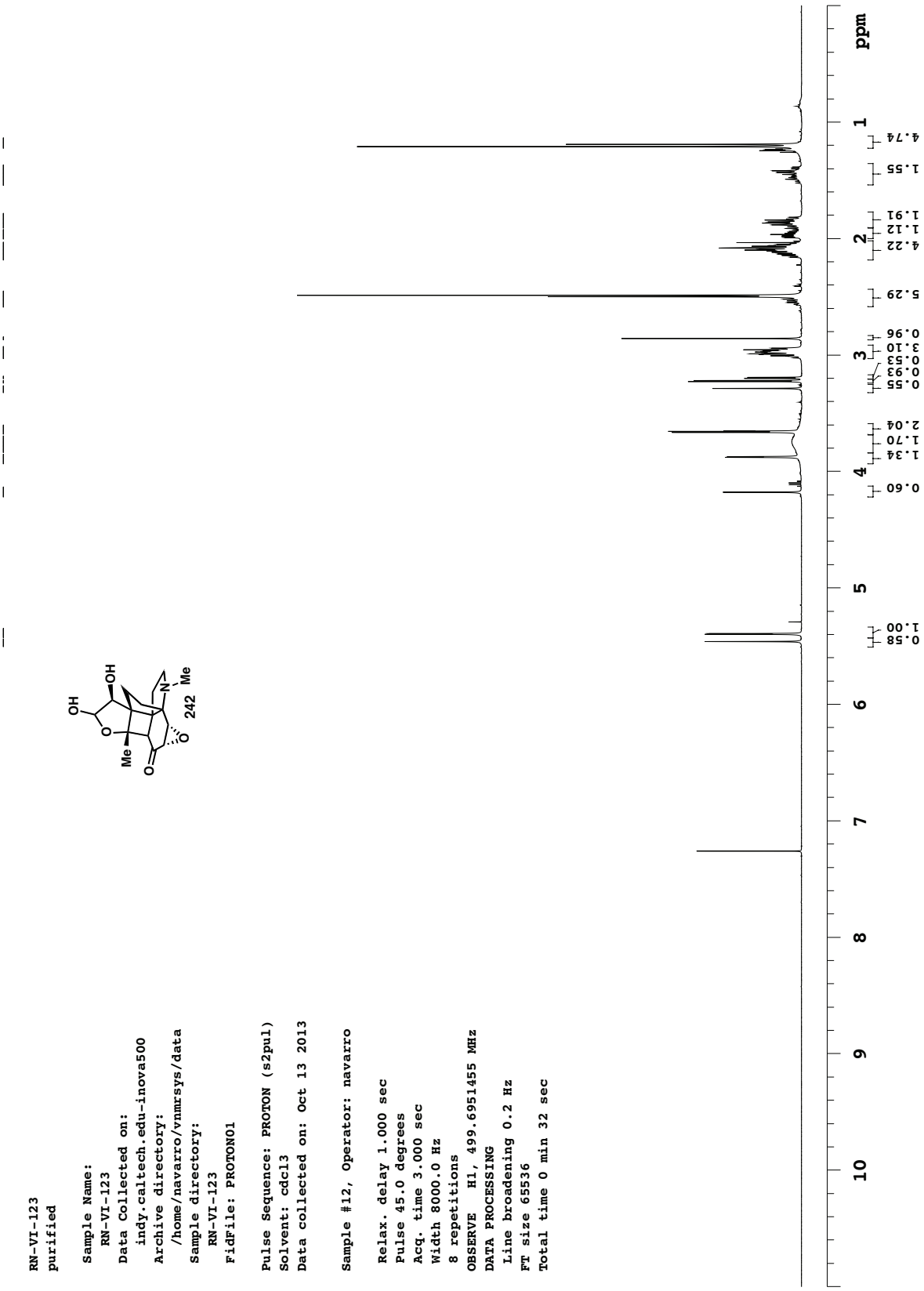
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
12000 repetitions
OBSERVE C13, 125.6553271 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 6 hr, 50 min

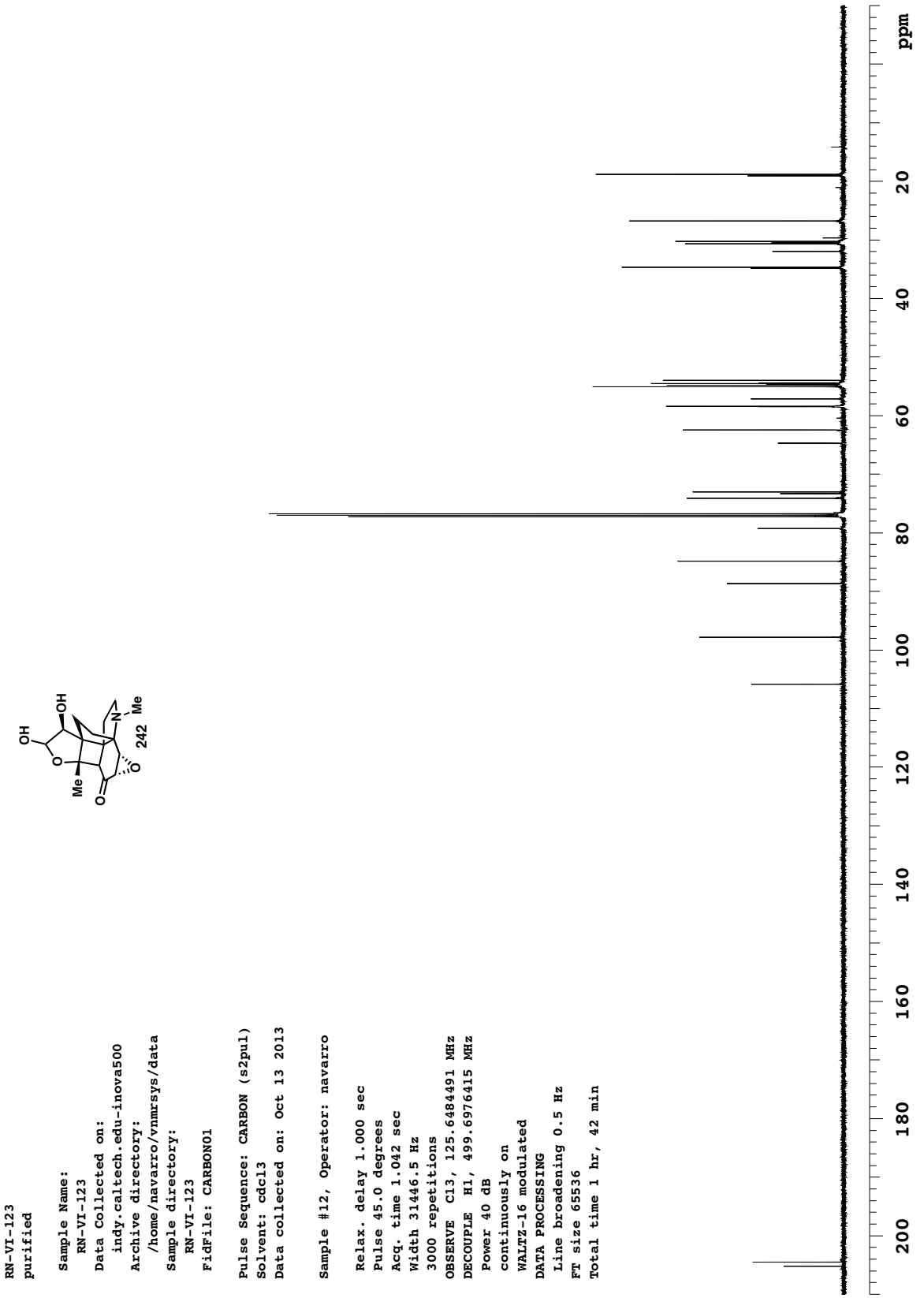


235

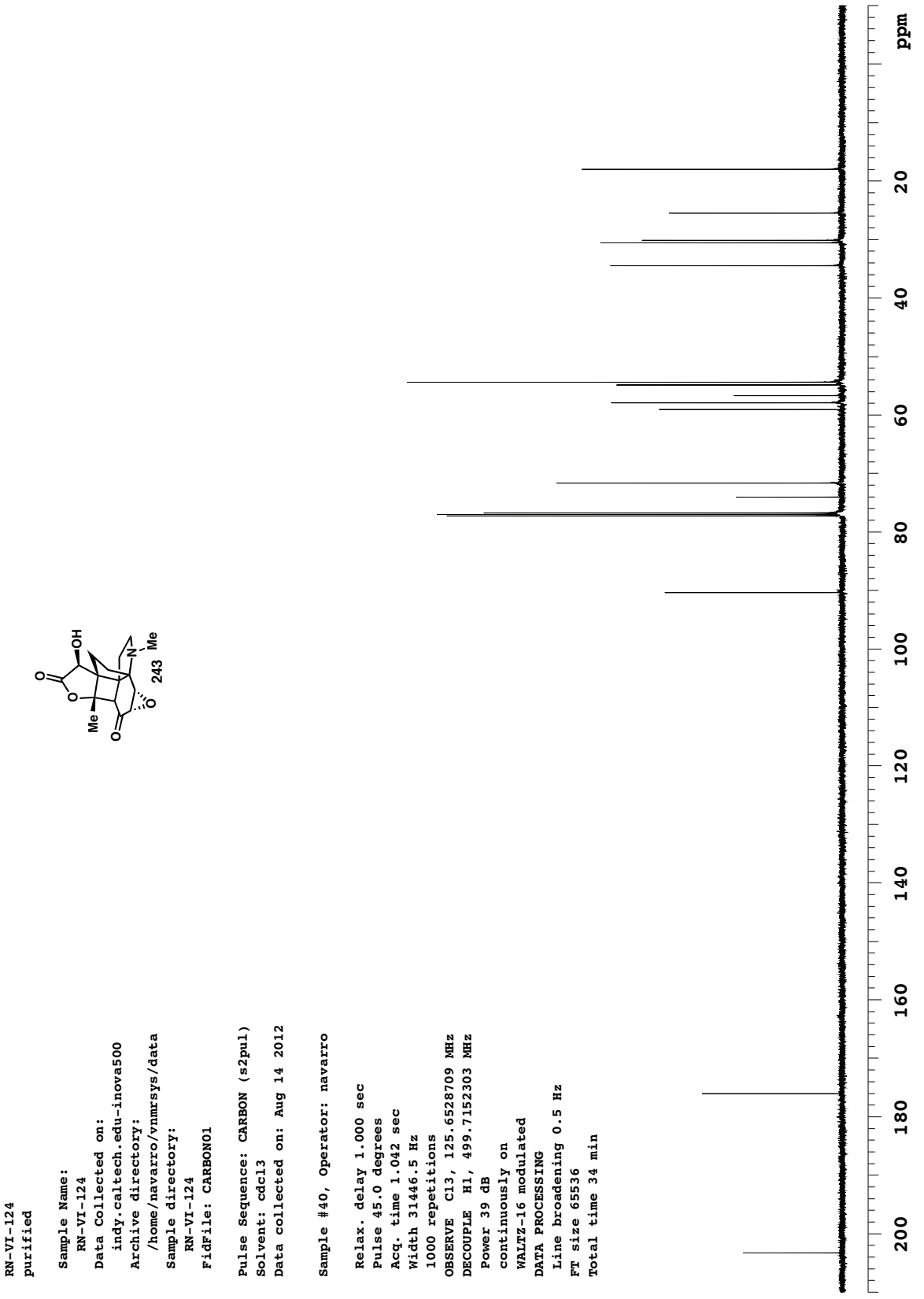

RN-V-100
flashed
Sample Name:
RN-V-100
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-100
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 26 2011
Sample #41, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7225128 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 28 sec
Me
O
O
O
HO
N
Me
238
ppm
1.03
3.17
0.96
1.13
2.16
3.38
1.21
1.04
4.20
1.16
1.12
1.82
1.00
1.00

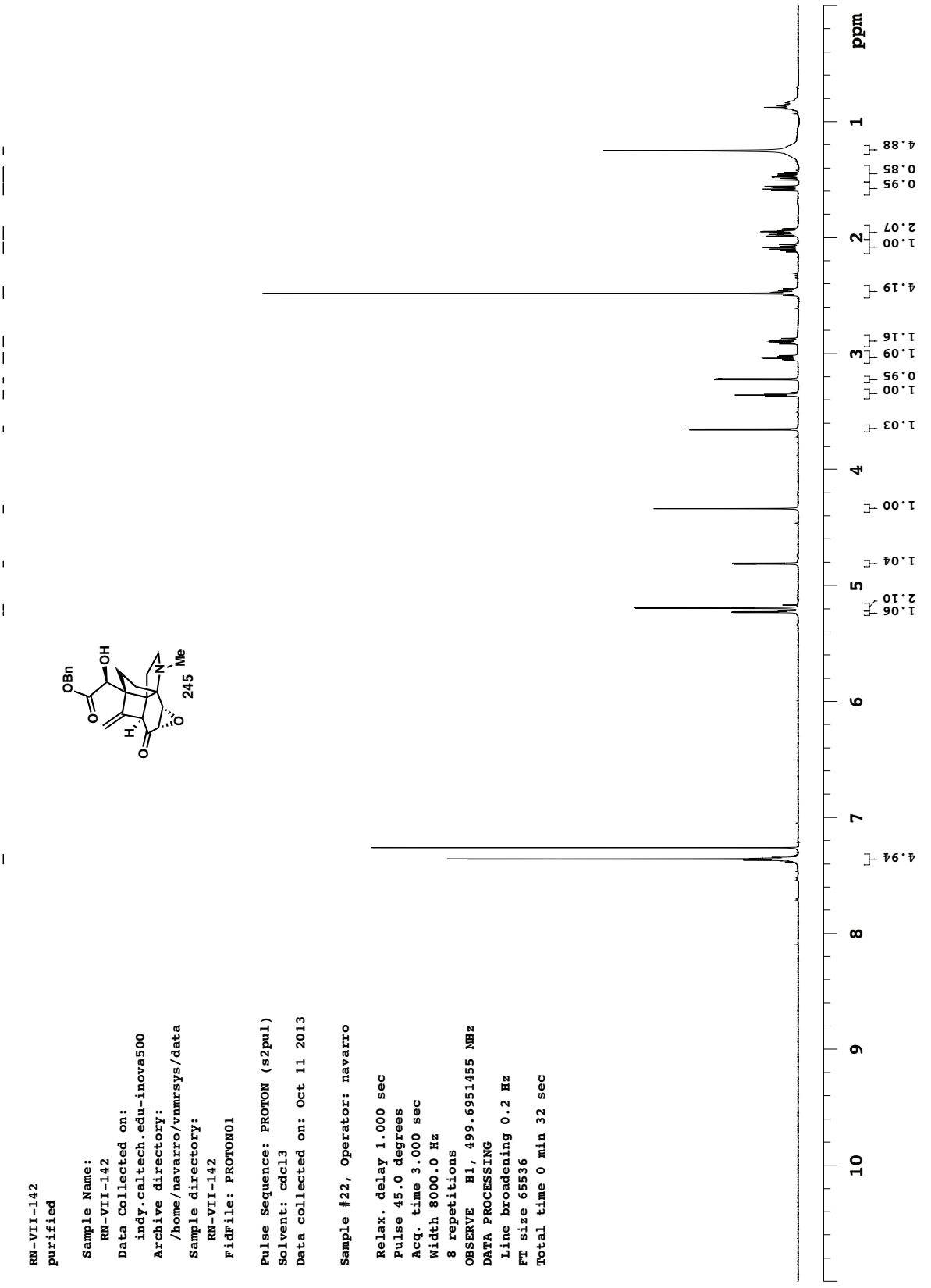

RN-V-100
flashed
Sample Name:
RN-V-100
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-V-100
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 27 2011
Sample #41, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
6000 repetitions
OBSERVE C13, 125.6553271 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 3 hr, 25 min
Me
O
O
O
HO
N
Me
238
200
180
160
140
120
100
80
60
40
20
ppm

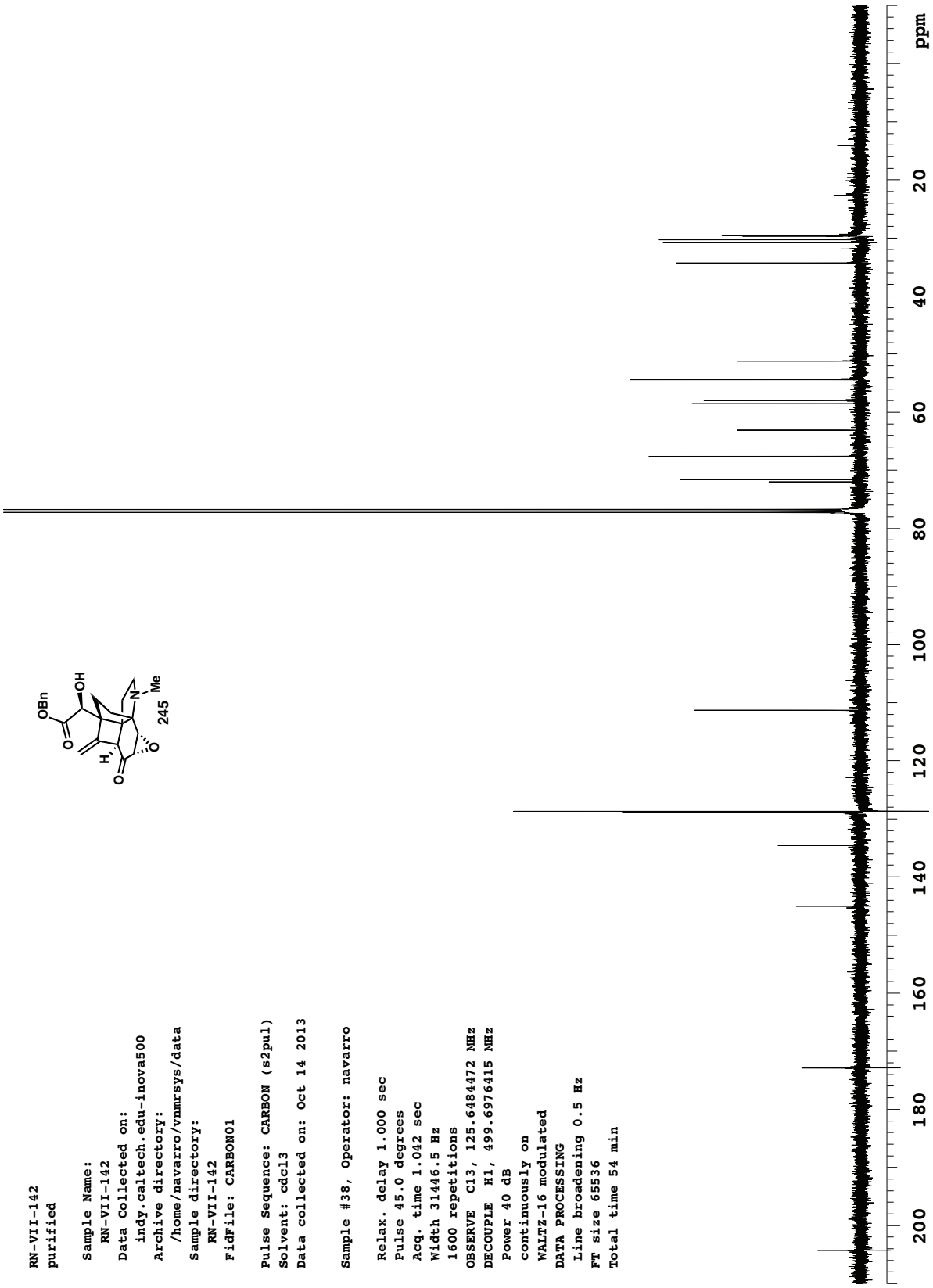

RN-VI-123
purified
Sample Name:
RN-VI-123
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-123
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 13 2013
Sample #12, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.6951455 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 32 sec
OH
OH
Me
O
O
O
N
Me
242
ppm
0.58
1.00
0.60
1.34
1.70
2.04
0.55
0.93
0.53
3.10
0.96
5.29
4.22
1.12
1.91
1.55
4.74

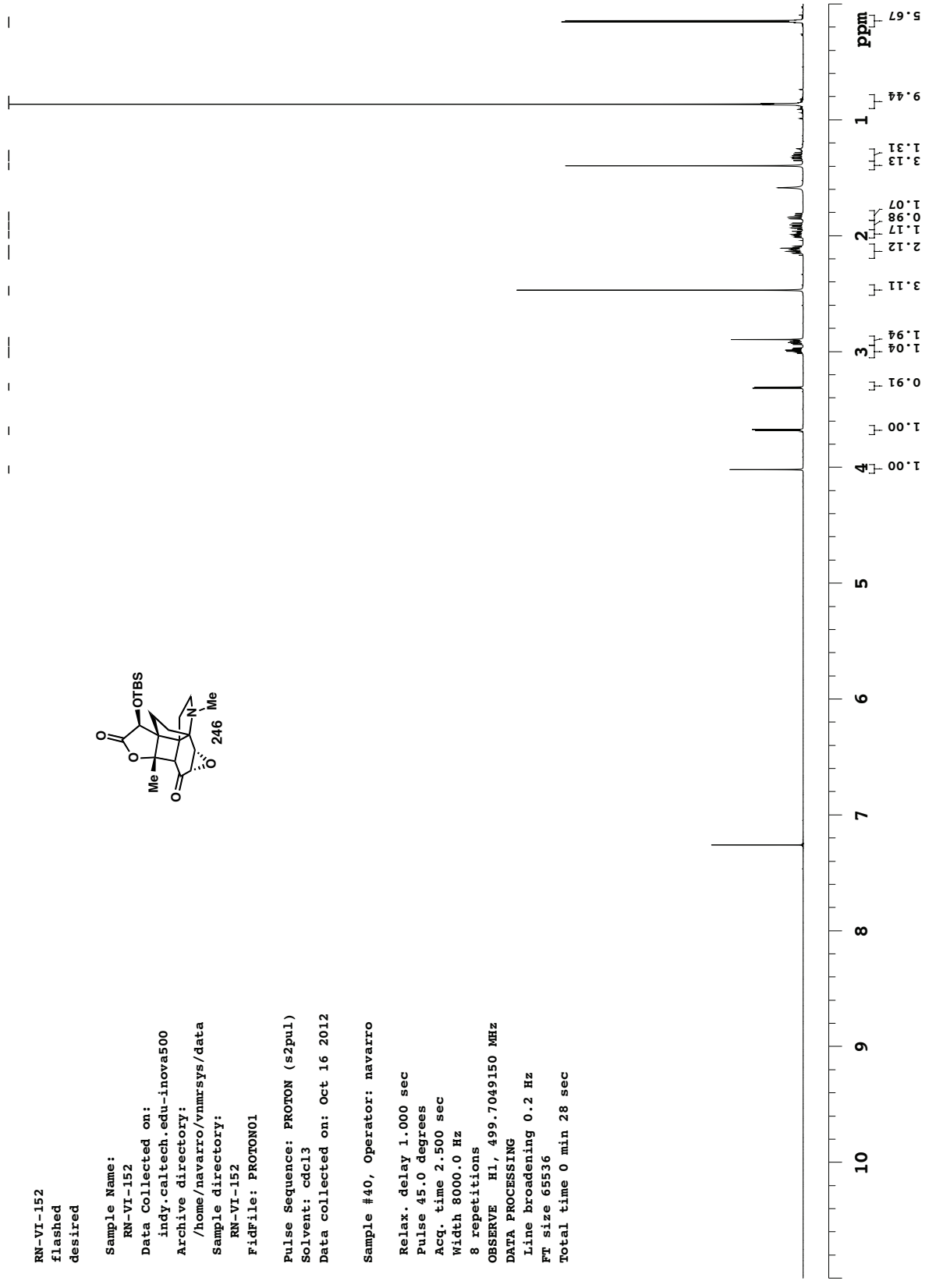

RN-VI-123
purified
Sample Name:
RN-VI-123
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-123
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 13 2013
Sample #12, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
3000 repetitions
OBSERVE C13, 125.6484491 MHz
DECOUPLE H1, 499.6976415 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 42 min
OH
OH
Me
O
O
O
N
Me
242
200
180
160
140
120
100
80
60
40
20
ppm

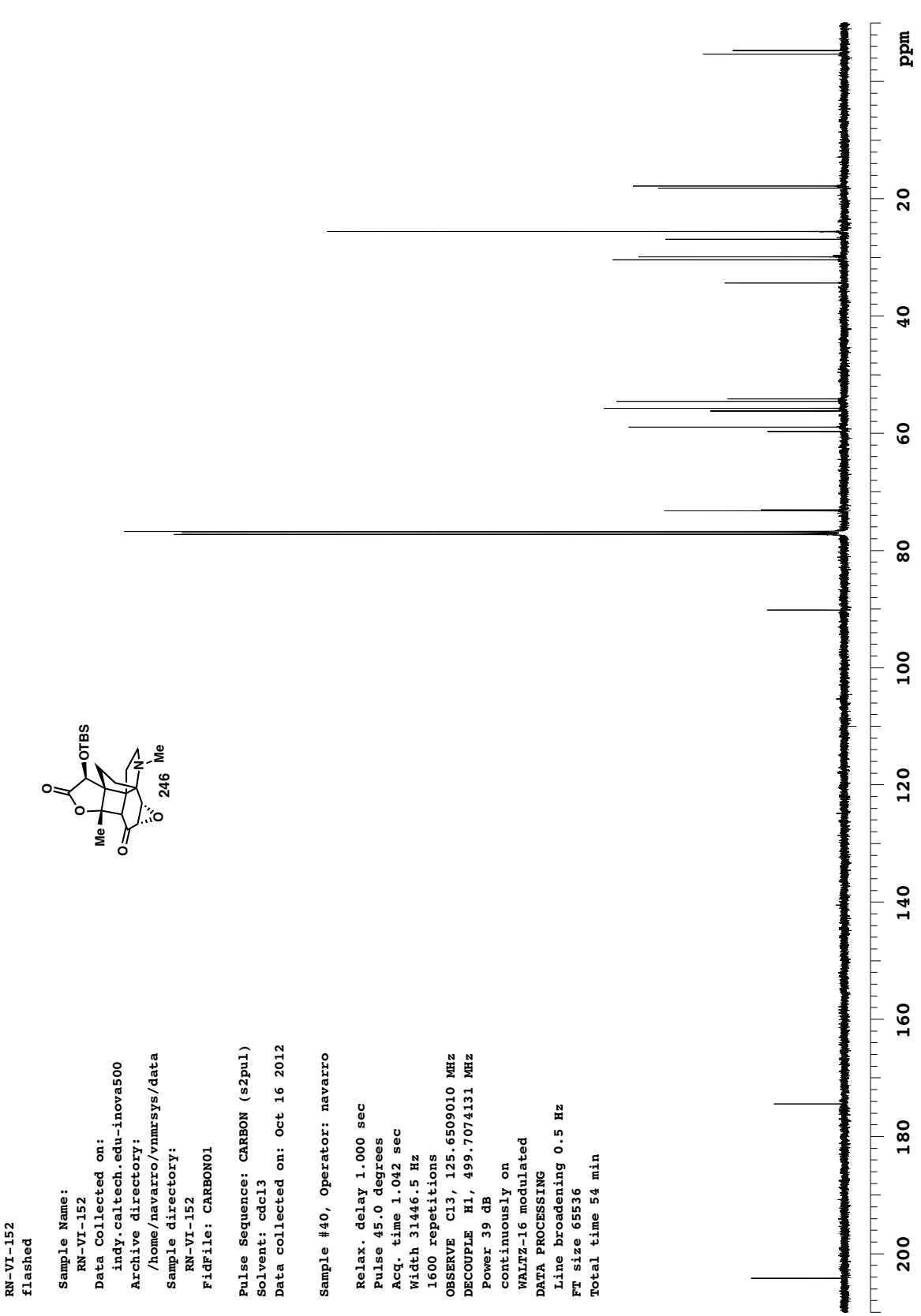
RN-VI-124
purified
Sample Name:
RN-VI-124
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-124
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 14 2012
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7127429 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 28 sec
OH
O
O
Me
O
O
N
Me
243
ppm
0.93
1.00
1.06
1.06
0.92
1.05
0.94
3.13
1.07
1.18
1.98
1.07
4.03

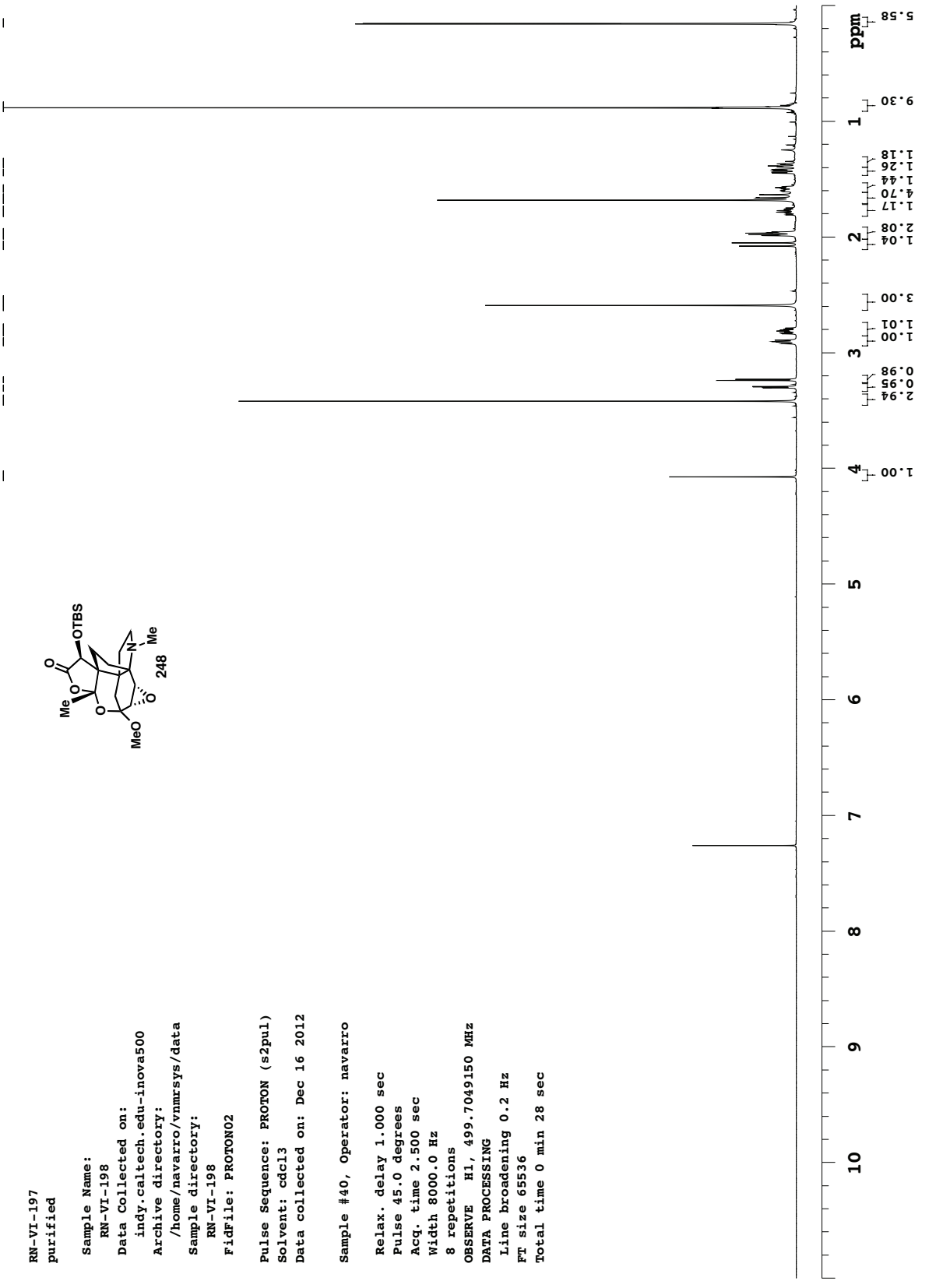

RN-VI-124
purified
Sample Name:
RN-VI-124
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-124
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 14 2012
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6528709 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
OH
N
Me
243 Me
O
O
O
Me
O
O
200
180
160
140
120
100
80
60
40
20
ppm

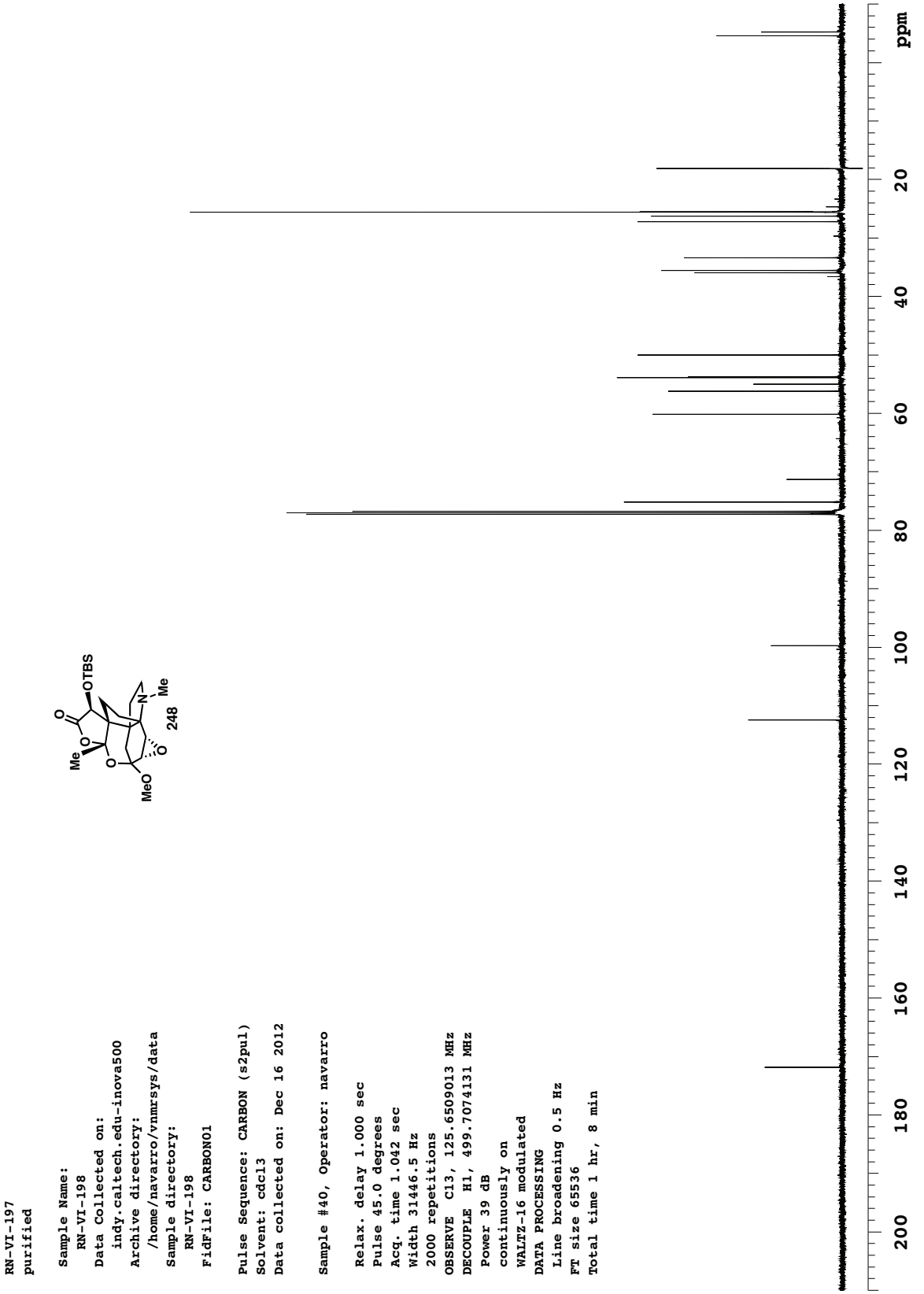

RN-VII-142
purified
Sample Name:
RN-VII-142
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VII-142
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 11 2013
Sample #22, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.6951455 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 32 sec
OBn
OH
N
Me
245
O
H
ppm
4.94
1.06
2.10
1.04
1.00
1.03
1.00
0.95
1.09
1.16
4.19
1.00
2.07
0.95
0.85
4.88

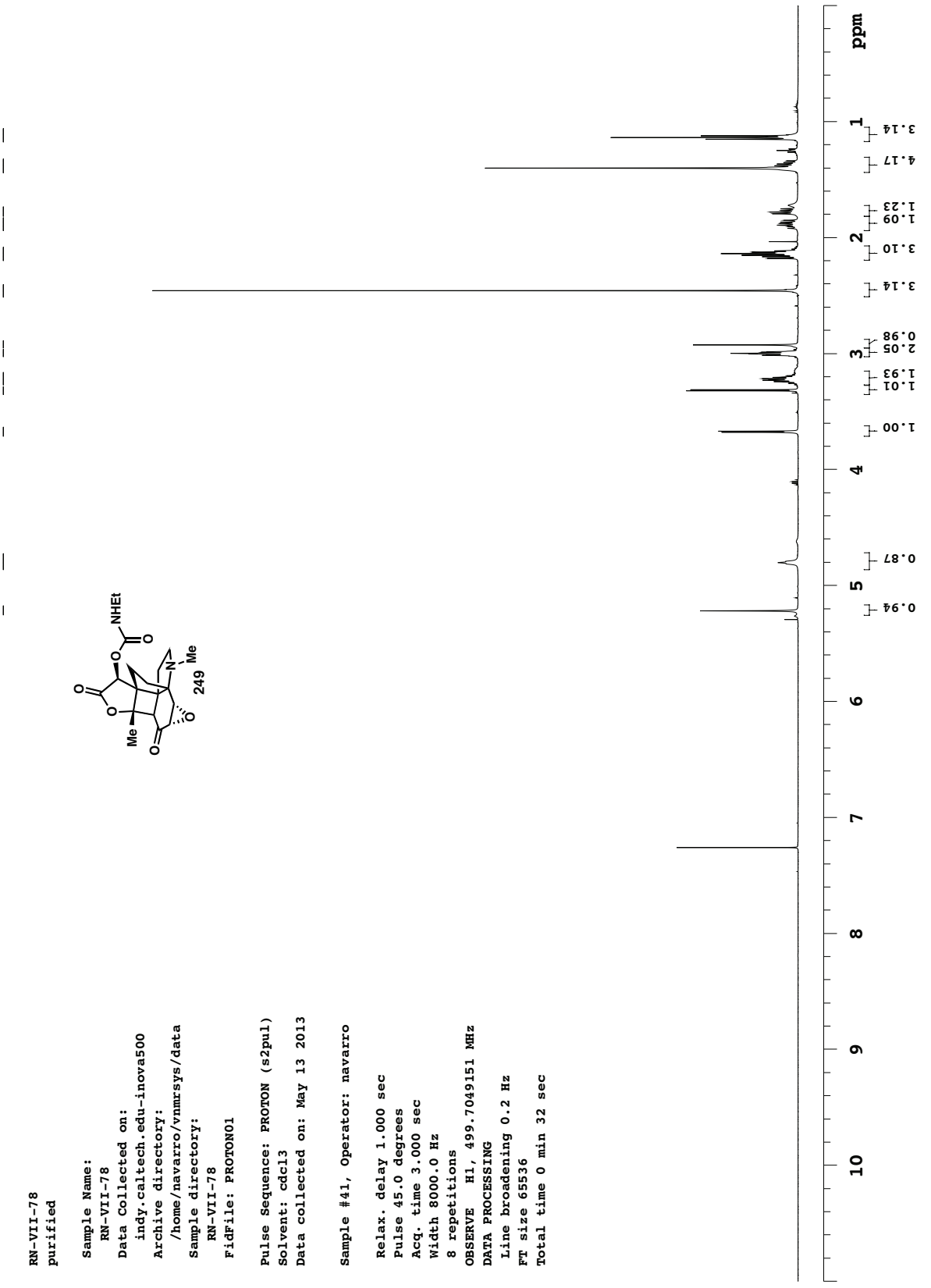

RN-VII-142
purified
Sample Name:
RN-VII-142
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VII-142
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 14 2013
Sample #38, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1600 repetitions
OBSERVE C13, 125.6484472 MHz
DECOUPLE H1, 499.6976415 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 54 min
OBn
OH
O
H
O
O
N
Me
245
200
180
160
140
120
100
80
60
40
20
ppm

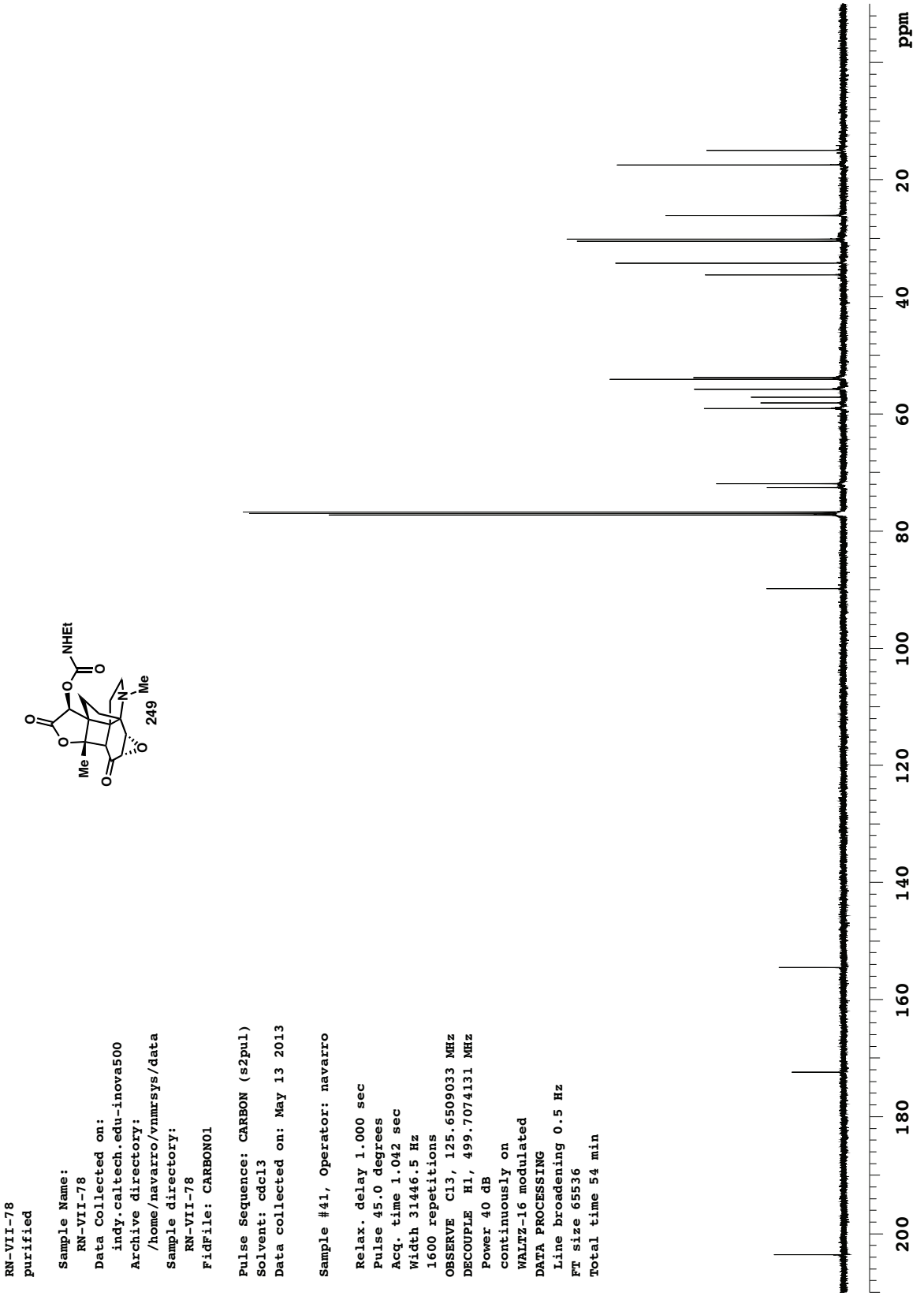

RN-VI-152
flashed
desired
Sample Name:
RN-VI-152
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-152
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 16 2012
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7049150 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 28 sec
OTBS
Me
N
Me
O
O
O
O
O
246
ppm
10
9
8
7
6
5
4
3
2
1
1.00
0.91
1.04
1.94
3.11
2.12
1.17
0.98
1.07
3.13
1.31
9.44
1.00
5.67


RN-VI-152
flashed
Sample Name:
RN-VI-152
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-152
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 16 2012
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1600 repetitions
OBSERVE C13, 125.6509010 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 54 min
OTBS
Me
N
Me
O
O
O
O
O
246
200
180
160
140
120
100
80
60
40
20
ppm


RN-VI-197
purified
Sample Name:
RN-VI-198
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-198
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Dec 16 2012
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7049150 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 28 sec
OTBS
Me
MeO
248
ppm
1.00
2.94
0.95
0.98
1.00
1.01
3.00
1.04
2.08
1.17
4.70
1.44
1.26
1.18
9.30
5.58


RN-VI-197
purified
Sample Name:
RN-VI-198
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-198
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Dec 16 2012
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2000 repetitions
OBSERVE C13, 125.6509013 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 8 min
OTBS
Me
MeO
Me
248
200
180
160
140
120
100
80
60
40
20
ppm


RN-VII-78
purified
Sample Name:
RN-VII-78
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VII-78
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 13 2013
Sample #41, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7049151 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 32 sec
NHEt
Me
Me
249
ppm
10
9
8
7
6
5
4
3
2
1
0.94
0.87
1.00
1.01
1.93
2.05
0.98
3.14
3.10
1.09
1.23
4.17
3.14


RN-VII-78
purified
Sample Name:
RN-VII-78
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VII-78
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 13 2013
Sample #41, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1600 repetitions
OBSERVE C13, 125.6509033 MHz
DECOUPLE H1, 499.7074131 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 54 min
NHEt
Me
Me
249
200
180
160
140
120
100
80
60
40
20
ppm

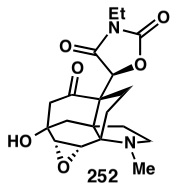
RN-VII-50
purified

Sample Name:
RN-VII-50
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VII-50
FidFile: PROTON01

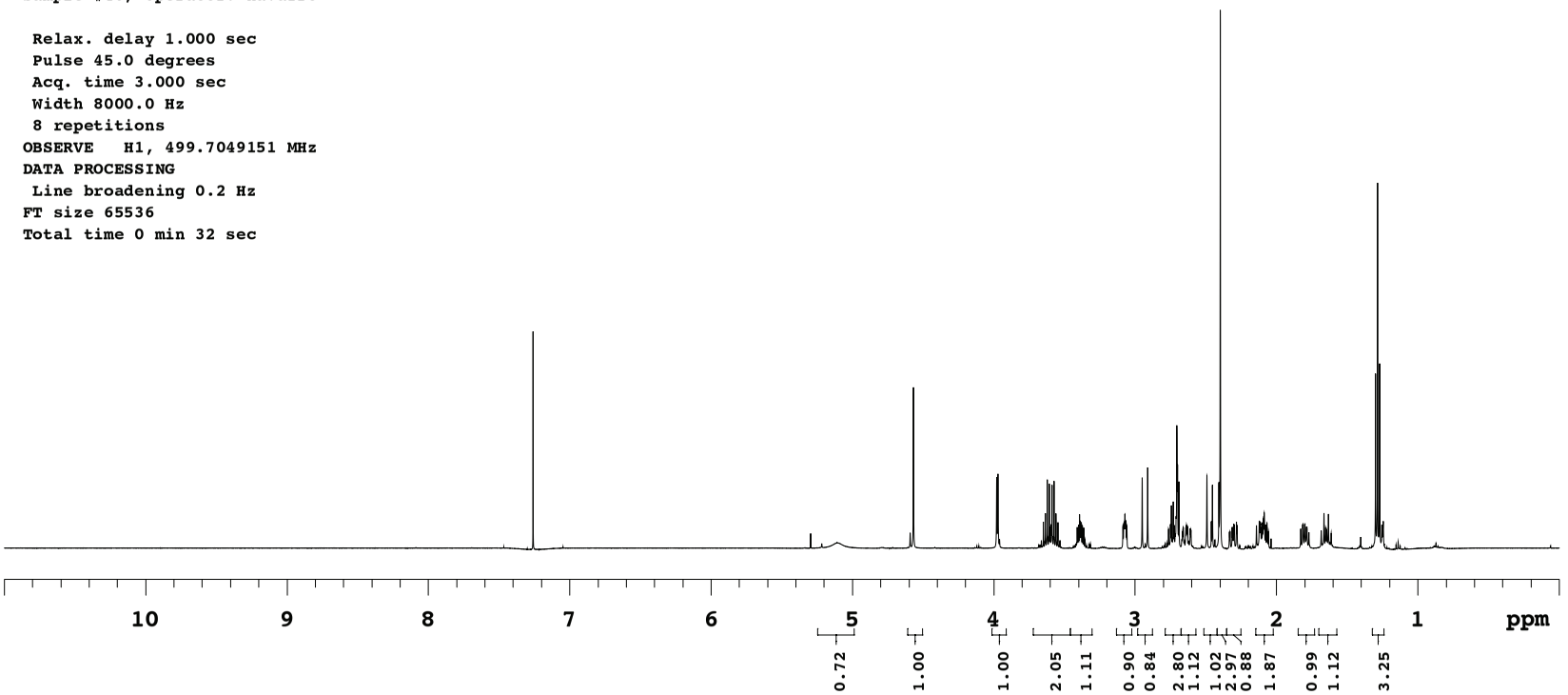
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 3 2013

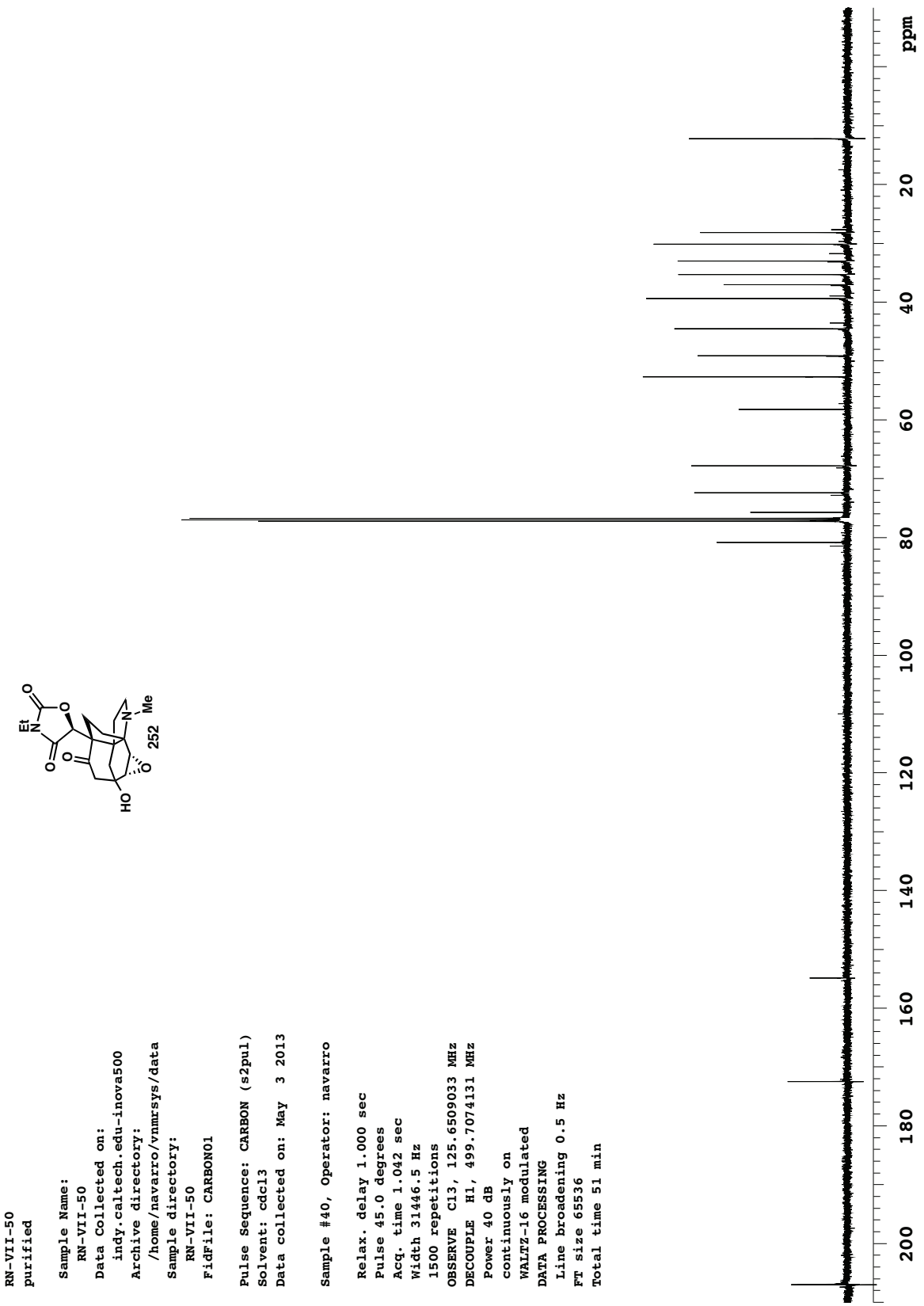
Sample #40, Operator: navarro

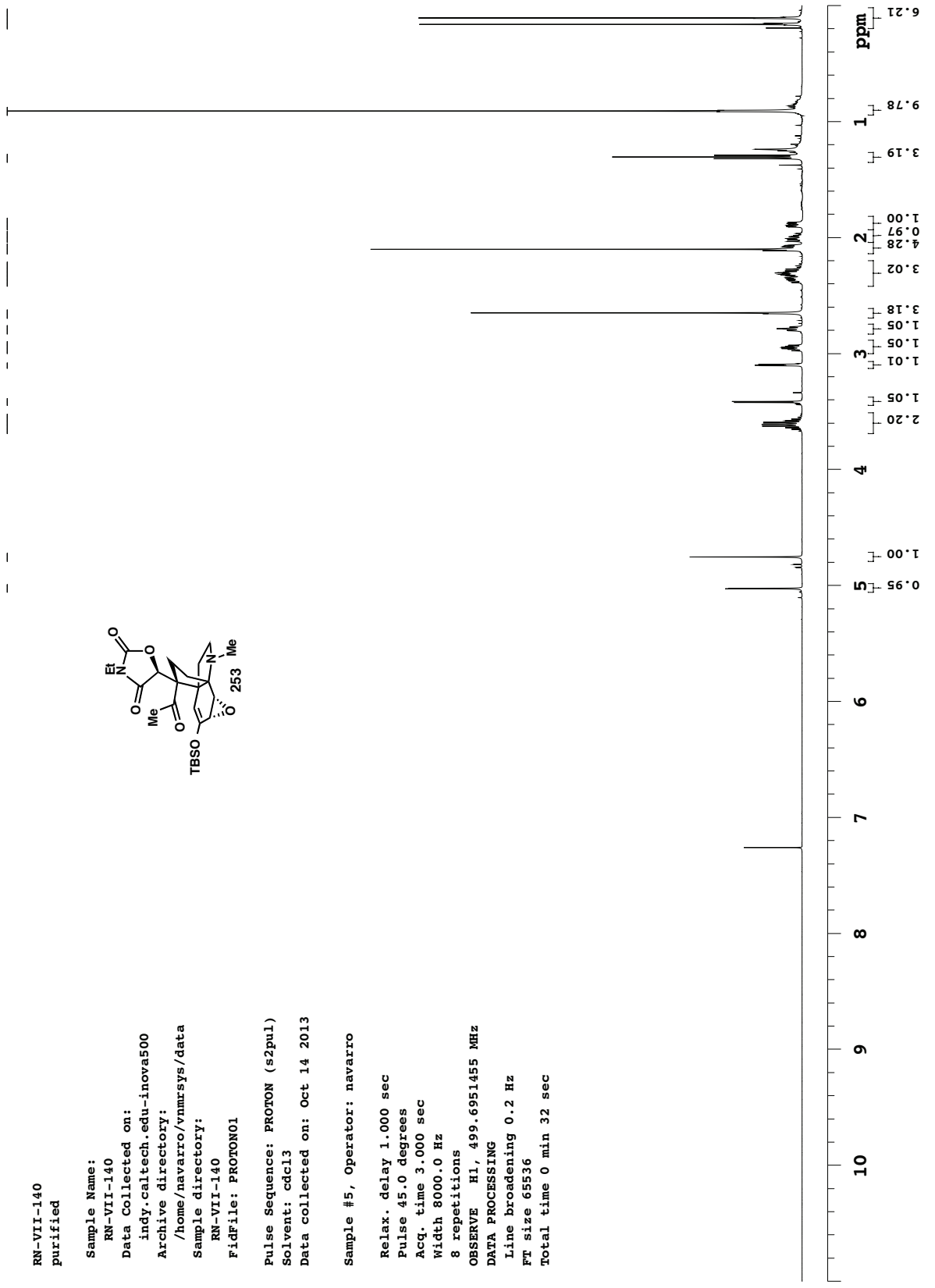
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7049151 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 32 sec

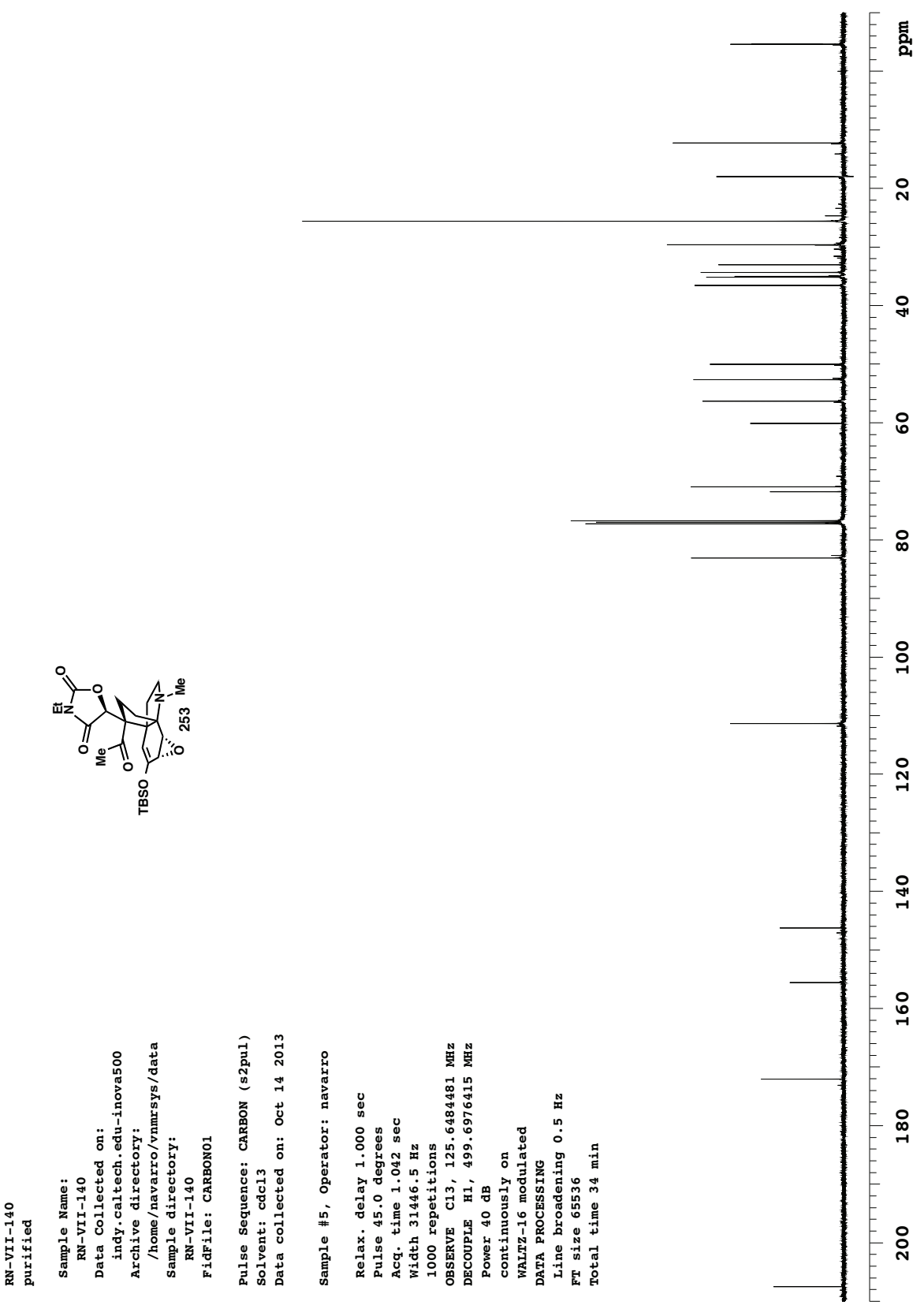


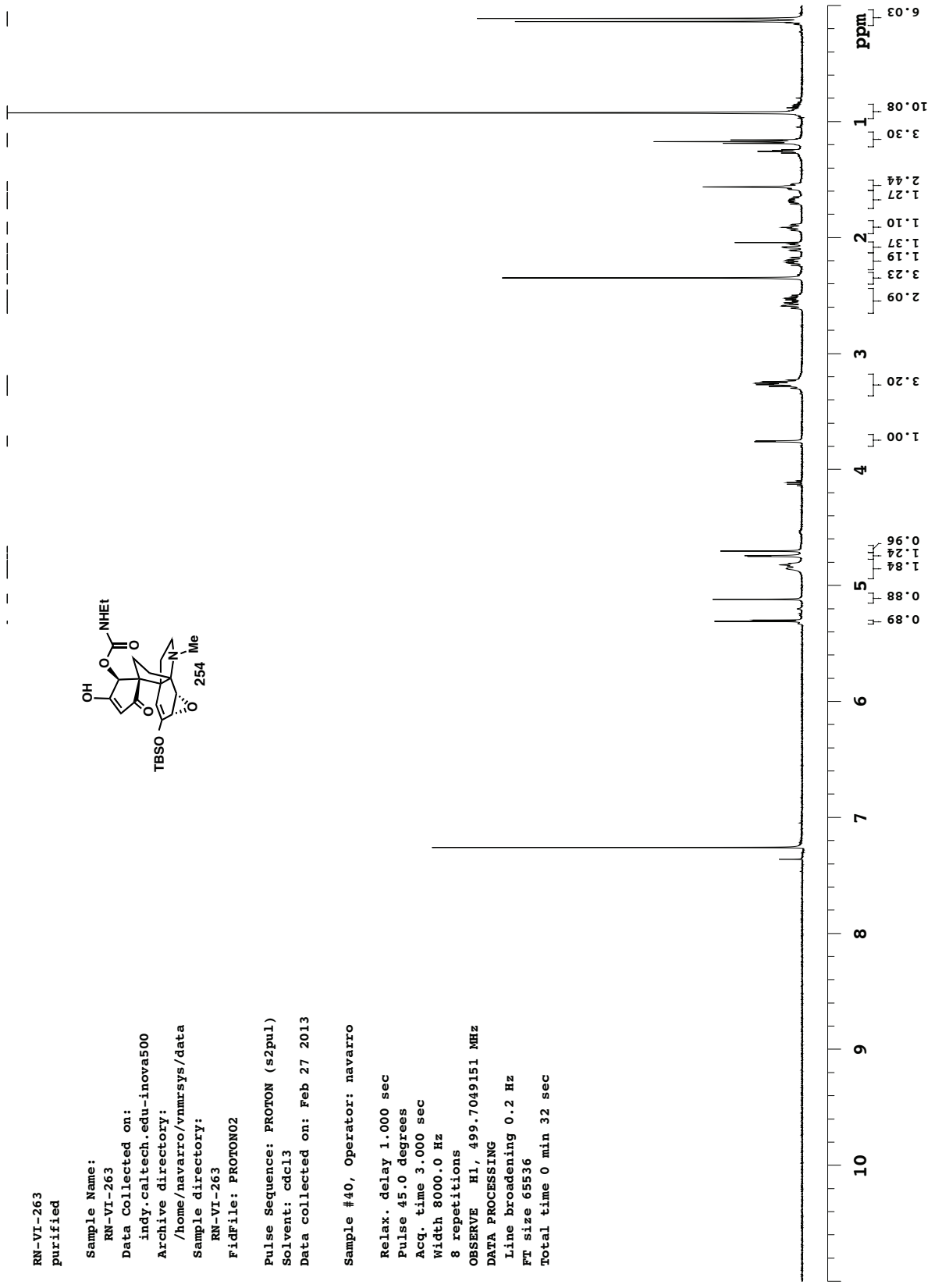
252

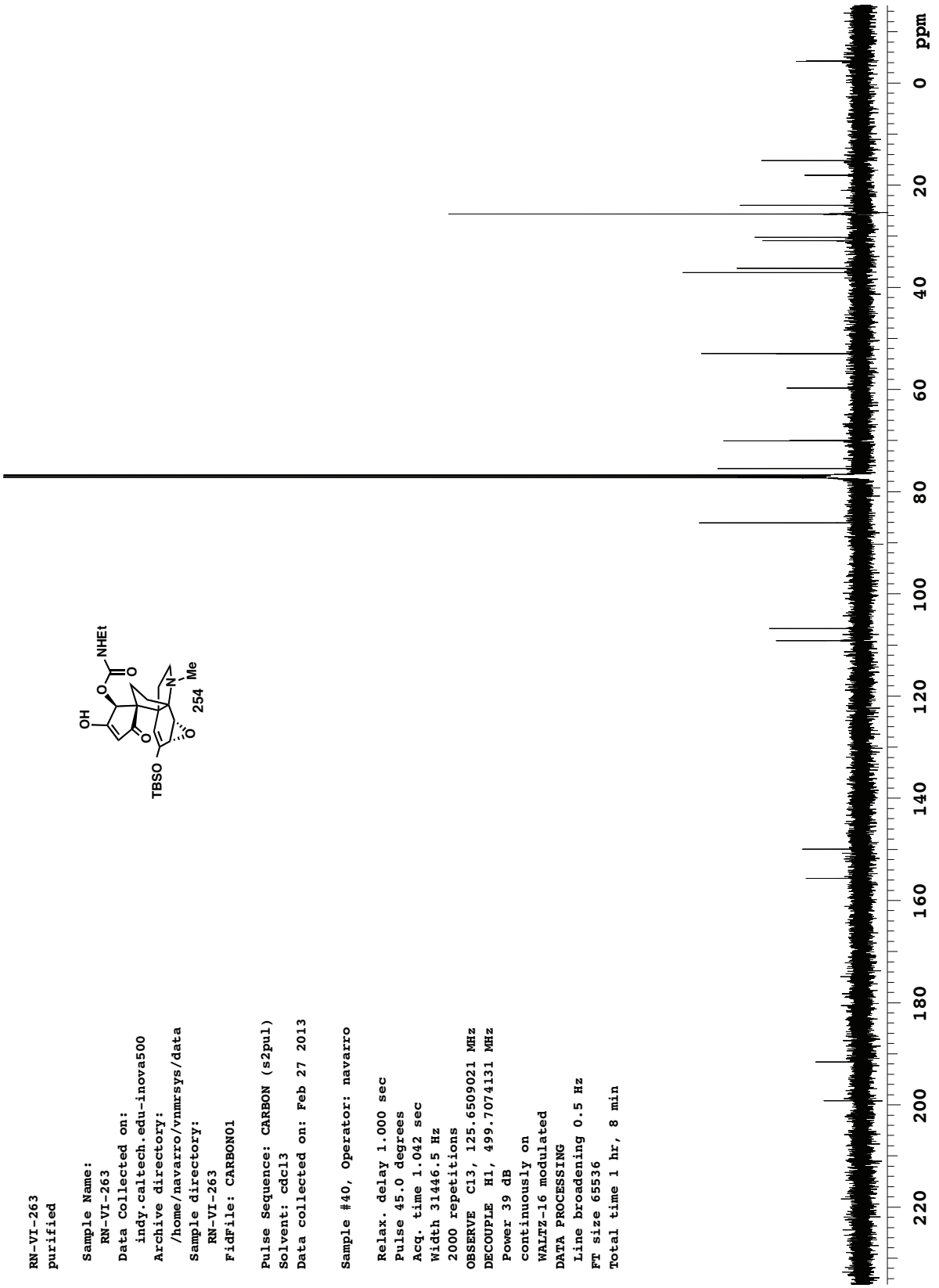


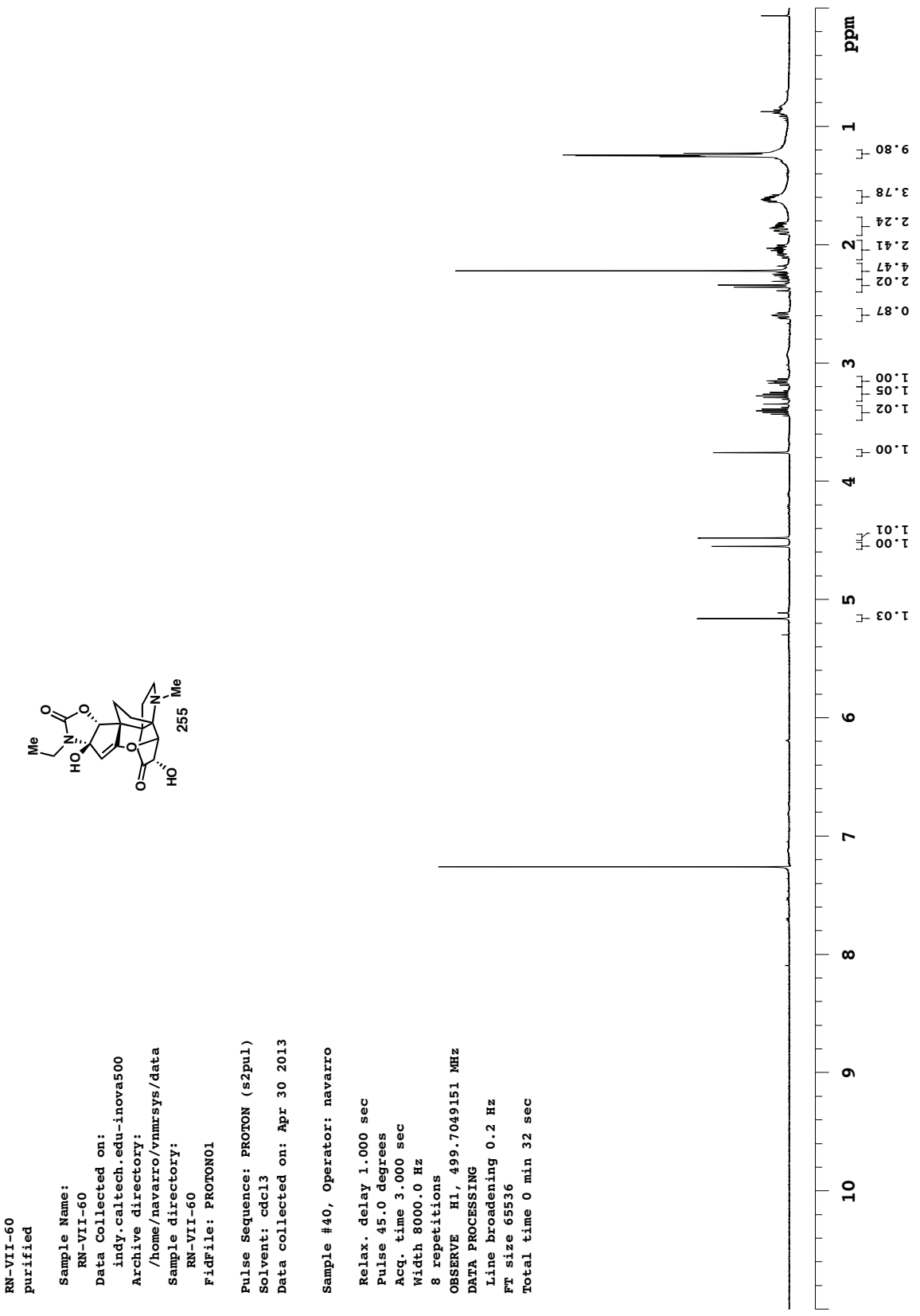

RN-VII-50
purified
Sample Name:
RN-VII-50
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VII-50
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 3 2013
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6509033 MHz
DECOUPLE H1, 499.7074131 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
Et
N
O
O
O
O
HO
O
N
Me
252
200
180
160
140
120
100
80
60
40
20
ppm

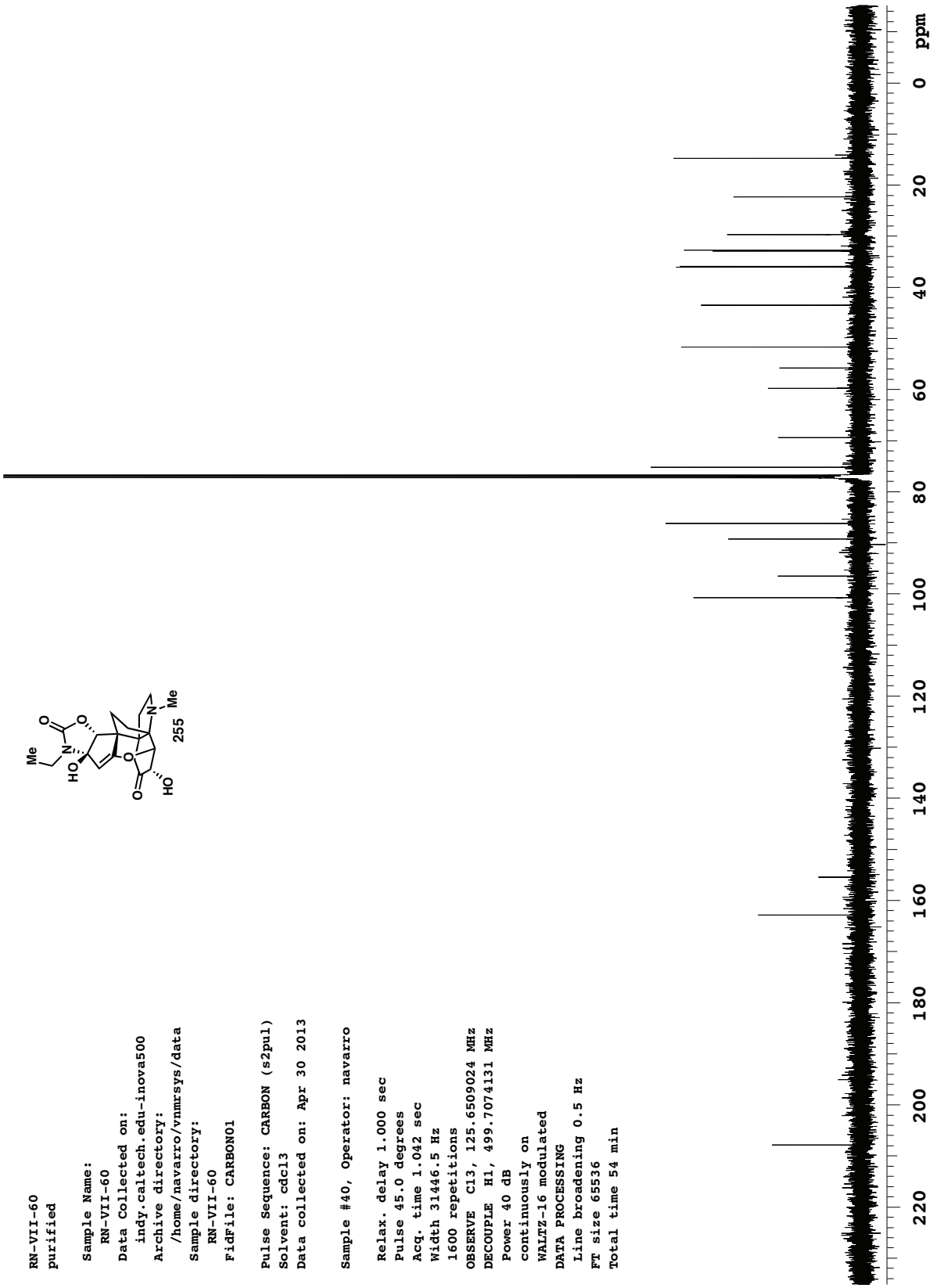

RN-VII-140
purified
Sample Name:
RN-VII-140
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VII-140
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 14 2013
Sample #5, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.6951455 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 32 sec
Et
Me
TBSO
Me
253
ppm
6.21
9.78
3.19
1.00
0.97
4.28
3.02
3.18
1.05
1.05
1.01
2.20
1.05
1.00
0.95

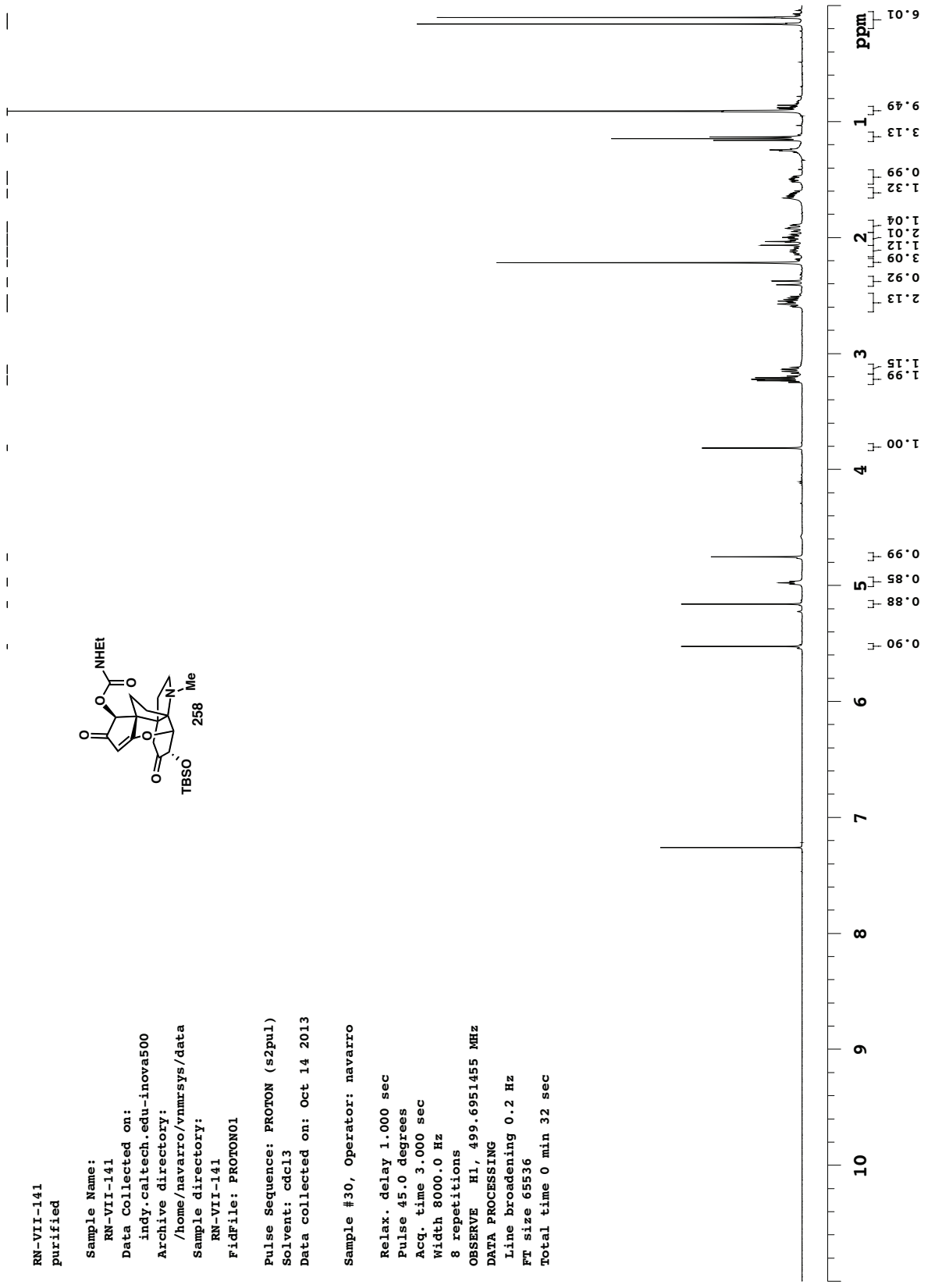

RN-VII-140
purified
Sample Name:
RN-VII-140
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VII-140
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 14 2013
Sample #5, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6484481 MHz
DECOUPLE H1, 499.6976415 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
Et
N
O
O
O
O
Me
O
TBSO
O
N
Me
253
200
180
160
140
120
100
80
60
40
20
ppm

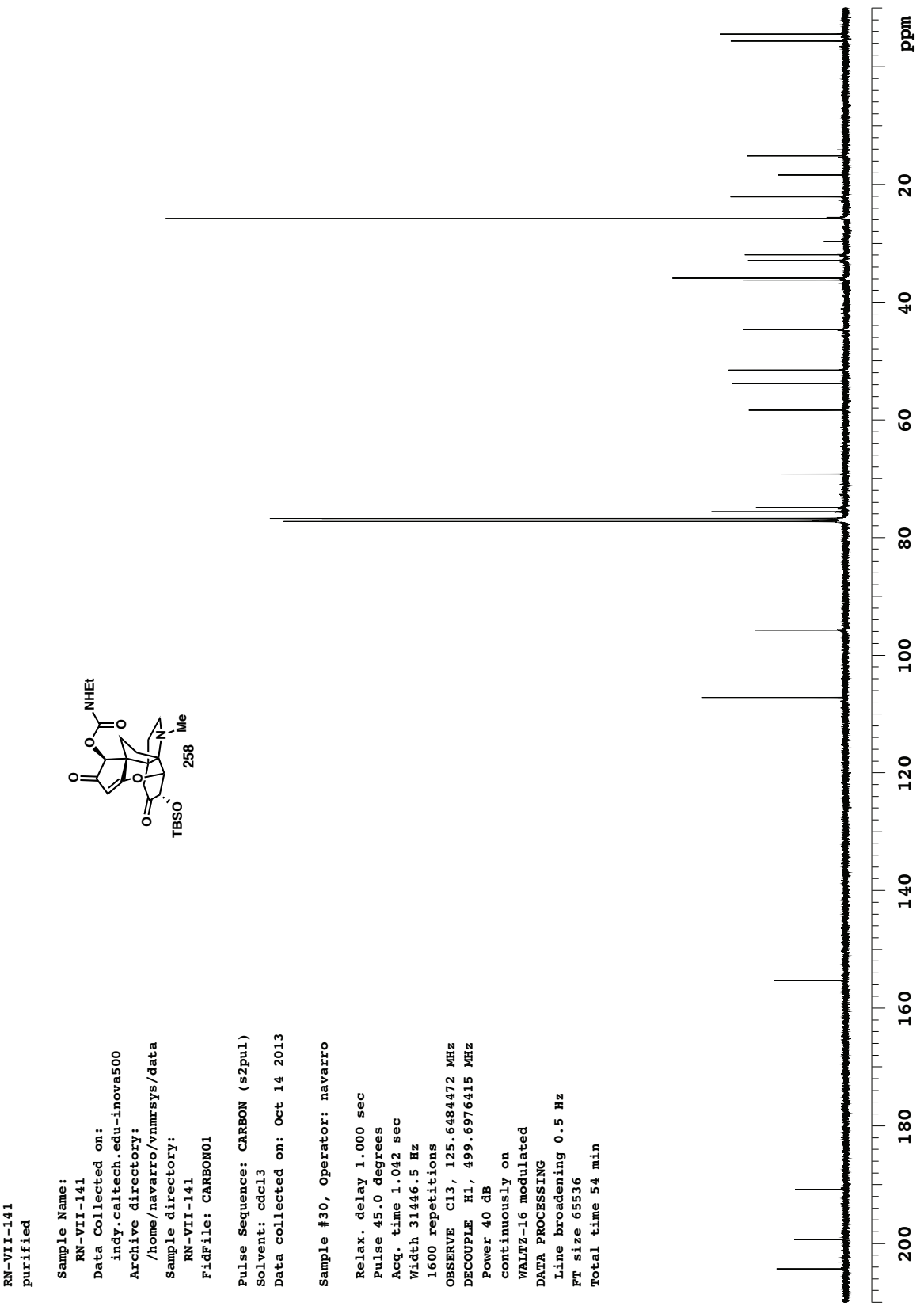

RN-VI-263
purified
Sample Name:
RN-VI-263
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-263
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Feb 27 2013
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7049151 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 32 sec
NHEt
OH
TBSO
Me
254
ppm
10.08
3.30
2.44
1.27
1.10
2.09
3.23
1.19
1.37
3.20
1.00
0.96
1.24
1.84
0.88
0.89


RN-VI-263
purified
Sample Name:
RN-VI-263
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VI-263
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Feb 27 2013
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2000 repetitions
OBSERVE C13, 125.6509021 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 8 min
NHEt
OH
TBSO
N
Me
254
220
200
180
160
140
120
100
80
60
40
20
0
ppm


RN-VII-60
purified
Sample Name:
RN-VII-60
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VII-60
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 30 2013
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7049151 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 32 sec
Me
HO
255
Me
HO
ppm
9.80
3.78
2.24
2.41
4.47
2.02
0.87
1.00
1.05
1.02
1.00
1.00
1.01
1.03


RN-VII-60
purified
Sample Name:
RN-VII-60
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VII-60
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 30 2013
Sample #40, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1600 repetitions
OBSERVE C13, 125.6509024 MHz
DECOUPLE H1, 499.7074131 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 54 min
Me
HO
O
O
N
O
O
N
Me
HO
255
220
200
180
160
140
120
100
80
60
40
20
0
ppm


RN-VII-141
purified
Sample Name:
RN-VII-141
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VII-141
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 14 2013
Sample #30, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.6951455 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 32 sec
NHEt
O
O
O
O
O
N
Me
TBSO
258
ppm
10
9
8
7
6
5
4
3
2
1
0.90
0.88
0.85
0.99
1.00
1.99
1.15
2.13
0.92
3.09
1.12
2.01
1.04
1.32
0.99
3.13
9.49
6.01


RN-VII-141
purified
Sample Name:
RN-VII-141
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/navarro/vnmrsys/data
Sample directory:
RN-VII-141
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 14 2013
Sample #30, Operator: navarro
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1600 repetitions
OBSERVE C13, 125.6484472 MHz
DECOUPLE H1, 499.6976415 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 54 min
NHEt
O
O
O
O
O
O
TBSO
N
Me
258
200
180
160
140
120
100
80
60
40
20
ppm

APPENDIX 4

X-Ray Crystallography Reports Relevant to Chapter 4:

Progress Toward the Total Synthesis of Acutumine[†]

[†] The work disclosed in this appendix for the X-ray crystallographic analysis of **230**, **238**, and **255** was completed entirely by Larry Henling and Dr. Michael Day in the Caltech X-ray crystallography lab.

A4.1. Crystal Structure analysis of bromohydrin 230.

Figure A4.1. Bromohydrin **230**. Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition number 821739.

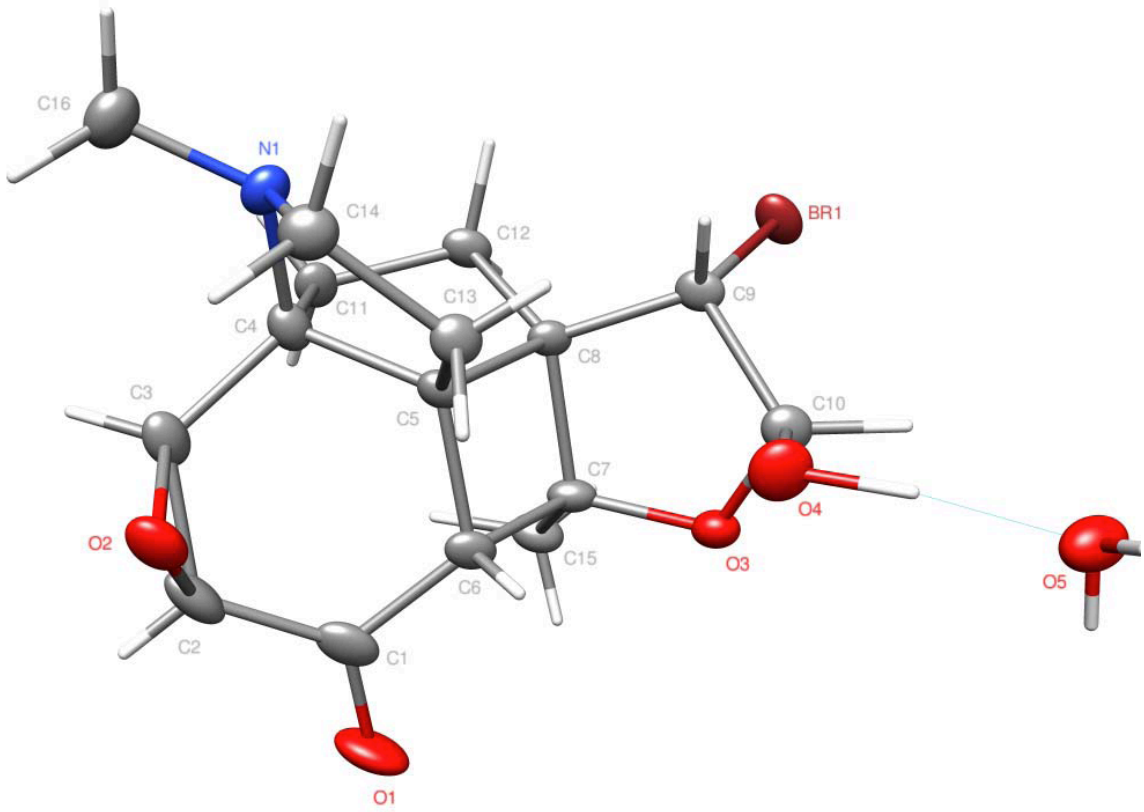


Table A4.1. Crystal data and structure refinement for bromohydrin **230**.

Empirical formula	$C_{16}H_{20}BrNO_4 \bullet H_2O$
Formula weight	388.26
Crystallization Solvent	Diethyl ether/hexanes
Crystal Habit	Plate
Crystal size	0.41 x 0.21 x 0.02 mm^3
Crystal color	Colorless

Data Collection

Type of diffractometer	Bruker KAPPA APEX II	
Wavelength	0.71073 Å MoKα	
Data Collection Temperature	100(2) K	
θ range for 9272 reflections used in lattice determination	2.31 to 25.62°	
Unit cell dimensions	a = 7.2279(3) Å b = 12.4336(5) Å c = 17.6522(7) Å	α= 90° β= 90° γ = 90°
Volume	1586.38(11) $Å^3$	
Z	4	
Crystal system	Orthorhombic	
Space group	$P\ 2_12_12_1$	
Density (calculated)	1.626 Mg/m^3	
F(000)	800	
Data collection program	Bruker APEX2 v2009.7-0	
θ range for data collection	2.00 to 32.34°	
Completeness to θ = 32.34°	96.5 %	
Index ranges	$-10 \le h \le 10$, $-18 \le k \le 18$, $-26 \le l \le 25$	
Data collection scan type	ω scans; 10 settings	
Data reduction program	Bruker SAINT-Plus v7.66A	
Reflections collected	40470	
Independent reflections	5378 [R_{int}= 0.0867]	
Absorption coefficient	2.617 mm^{-1}	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7464 and 0.5033	

Table A4.1. (continued)

Structure solution and Refinement

Structure solution program	SHELXS-97 (Sheldrick, 2008)
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Difference Fourier map
Structure refinement program	SHELXL-97 (Sheldrick, 2008)
Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	5378 / 0 / 296
Treatment of hydrogen atoms	Unrestrained
Goodness-of-fit on F^2	1.446
Final R indices [$I>2\sigma(I)$, 4263 reflections]	R1 = 0.0481, *w*R2 = 0.0693
R indices (all data)	R1 = 0.0722, *w*R2 = 0.0719
Type of weighting scheme used	Sigma
Weighting scheme used	$w=1/\sigma^2(Fo^2)$
Max shift/error	0.002
Average shift/error	0.000
Absolute structure determination	Anomalous differences
Absolute structure parameter	0.014(8)
Largest diff. peak and hole	1.337 and -1.269 e.Å^{-3}

Special Refinement Details

Crystals were mounted on a glass fiber using Paratone oil then placed on the diffractometer under a nitrogen stream at 100K.

Refinement of F^2 against ALL reflections. The weighted R-factor (*w*R) and goodness of fit (S) are based on F^2, conventional R-factors (R) are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R-factors based on ALL data will be even larger.

All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Table A4.2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for RUN03 (CCDC 821739). U(eq) is defined as the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
Br(1)	2711(1)	7317(1)	6311(1)	22(1)
O(1)	10028(3)	9360(2)	8022(1)	35(1)
O(2)	10424(3)	10993(2)	6421(1)	26(1)
O(3)	6896(2)	7229(2)	7034(1)	19(1)
O(4)	8161(3)	6973(2)	5832(1)	27(1)
N(1)	6744(3)	10932(2)	5416(1)	20(1)
C(1)	9499(4)	9698(3)	7407(2)	24(1)
C(2)	9762(4)	10833(3)	7189(2)	26(1)
C(3)	8553(4)	11292(3)	6596(2)	21(1)
C(4)	7033(3)	10649(2)	6224(2)	18(1)
C(5)	7549(3)	9440(2)	6164(1)	15(1)
C(6)	8568(4)	8965(3)	6854(2)	17(1)
C(7)	6774(4)	8365(2)	7124(2)	17(1)
C(8)	5722(3)	8816(2)	6408(2)	14(1)
C(9)	5200(3)	7802(3)	5993(2)	16(1)
C(10)	6550(3)	6935(2)	6265(2)	19(1)
C(11)	5229(4)	10722(3)	6674(2)	19(1)
C(12)	4221(4)	9662(3)	6521(2)	18(1)
C(13)	8419(4)	9312(2)	5377(2)	17(1)
C(14)	8237(4)	10395(3)	4995(2)	22(1)
C(15)	6041(4)	8593(3)	7910(2)	22(1)
C(16)	6597(5)	12081(3)	5251(2)	28(1)
O(5)	8790(3)	4904(2)	5492(2)	28(1)

Table A4.3. Bond lengths [Å] and angles [°] for RUN03 (CCDC 821739).

Br(1)-C(9)	1.979(2)	C(7)-O(3)-C(10)	110.4(2)
O(1)-C(1)	1.225(4)	C(10)-O(4)-H(4)	100.3(19)
O(2)-C(3)	1.437(3)	C(16)-N(1)-C(14)	113.3(2)
O(2)-C(2)	1.452(4)	C(16)-N(1)-C(4)	115.7(2)
O(3)-C(7)	1.424(3)	C(14)-N(1)-C(4)	105.9(2)
O(3)-C(10)	1.429(3)	O(1)-C(1)-C(2)	121.3(3)
O(4)-C(10)	1.394(3)	O(1)-C(1)-C(6)	120.6(3)
O(4)-H(4)	1.14(4)	C(2)-C(1)-C(6)	118.1(3)
N(1)-C(16)	1.462(4)	O(2)-C(2)-C(1)	114.7(3)
N(1)-C(14)	1.471(4)	O(2)-C(2)-C(3)	58.70(19)
N(1)-C(4)	1.482(4)	C(1)-C(2)-C(3)	118.6(3)
C(1)-C(2)	1.475(5)	O(2)-C(2)-H(2)	110(2)
C(1)-C(6)	1.495(4)	C(1)-C(2)-H(2)	119(2)
C(2)-C(3)	1.479(5)	C(3)-C(2)-H(2)	120(2)
C(2)-H(2)	0.86(3)	O(2)-C(3)-C(2)	59.73(19)
C(3)-C(4)	1.509(4)	O(2)-C(3)-C(4)	117.0(2)
C(3)-H(3)	0.93(3)	C(2)-C(3)-C(4)	122.3(3)
C(4)-C(11)	1.530(4)	O(2)-C(3)-H(3)	110.7(16)
C(4)-C(5)	1.553(4)	C(2)-C(3)-H(3)	112.8(16)
C(5)-C(13)	1.533(3)	C(4)-C(3)-H(3)	119.5(16)
C(5)-C(6)	1.542(4)	N(1)-C(4)-C(3)	113.3(2)
C(5)-C(8)	1.591(3)	N(1)-C(4)-C(11)	111.4(2)
C(6)-C(7)	1.570(4)	C(3)-C(4)-C(11)	111.3(2)
C(6)-H(6)	0.80(3)	N(1)-C(4)-C(5)	101.4(2)
C(7)-C(15)	1.512(4)	C(3)-C(4)-C(5)	111.5(2)
C(7)-C(8)	1.578(4)	C(11)-C(4)-C(5)	107.3(2)
C(8)-C(9)	1.507(4)	C(13)-C(5)-C(6)	118.7(2)
C(8)-C(12)	1.524(4)	C(13)-C(5)-C(4)	105.1(2)
C(9)-C(10)	1.531(4)	C(6)-C(5)-C(4)	115.6(2)
C(9)-H(9)	0.85(3)	C(13)-C(5)-C(8)	122.4(2)
C(10)-H(10)	1.118(17)	C(6)-C(5)-C(8)	89.73(19)
C(11)-C(12)	1.529(4)	C(4)-C(5)-C(8)	104.72(19)
C(11)-H(11A)	0.98(3)	C(1)-C(6)-C(5)	119.8(3)
C(11)-H(11B)	0.86(3)	C(1)-C(6)-C(7)	117.6(2)
C(12)-H(12A)	0.97(3)	C(5)-C(6)-C(7)	91.6(2)
C(12)-H(12B)	1.05(3)	C(1)-C(6)-H(6)	109(2)
C(13)-C(14)	1.512(4)	C(5)-C(6)-H(6)	109(2)
C(13)-H(13A)	1.00(4)	C(7)-C(6)-H(6)	108(2)
C(13)-H(13B)	0.86(3)	O(3)-C(7)-C(15)	108.1(2)
C(14)-H(14A)	0.98(3)	O(3)-C(7)-C(6)	112.7(2)
C(14)-H(14B)	1.00(3)	C(15)-C(7)-C(6)	118.6(3)
C(15)-H(15A)	0.92(4)	O(3)-C(7)-C(8)	107.0(2)
C(15)-H(15B)	1.12(3)	C(15)-C(7)-C(8)	120.0(2)
C(15)-H(15C)	0.93(3)	C(6)-C(7)-C(8)	89.20(19)
C(16)-H(16A)	1.00(3)	C(9)-C(8)-C(12)	117.6(2)
C(16)-H(16B)	0.97(4)	C(9)-C(8)-C(7)	102.3(2)
C(16)-H(16C)	0.98(3)	C(12)-C(8)-C(7)	118.9(2)
O(5)-H(5A)	0.79(4)	C(9)-C(8)-C(5)	119.0(2)
O(5)-H(5B)	0.86(5)	C(12)-C(8)-C(5)	106.8(2)
		C(7)-C(8)-C(5)	89.46(18)
C(3)-O(2)-C(2)	61.6(2)	C(8)-C(9)-C(10)	106.1(2)

C(8)-C(9)-Br(1)	110.18(17)	C(14)-C(13)-H(13A)	111(2)
C(10)-C(9)-Br(1)	106.04(19)	C(5)-C(13)-H(13A)	114(2)
C(8)-C(9)-H(9)	112(2)	C(14)-C(13)-H(13B)	110.1(17)
C(10)-C(9)-H(9)	115.2(19)	C(5)-C(13)-H(13B)	112.6(17)
Br(1)-C(9)-H(9)	107.2(19)	H(13A)-C(13)-H(13B)	104(3)
O(4)-C(10)-O(3)	111.5(2)	N(1)-C(14)-C(13)	104.1(2)
O(4)-C(10)-C(9)	109.7(2)	N(1)-C(14)-H(14A)	108.3(19)
O(3)-C(10)-C(9)	103.3(2)	C(13)-C(14)-H(14A)	110.0(19)
O(4)-C(10)-H(10)	103.2(8)	N(1)-C(14)-H(14B)	103.5(19)
O(3)-C(10)-H(10)	111.7(9)	C(13)-C(14)-H(14B)	110.8(17)
C(9)-C(10)-H(10)	117.6(8)	H(14A)-C(14)-H(14B)	119(2)
C(12)-C(11)-C(4)	105.3(2)	C(7)-C(15)-H(15A)	109(2)
C(12)-C(11)-H(11A)	113.0(16)	C(7)-C(15)-H(15B)	114.7(15)
C(4)-C(11)-H(11A)	109.1(16)	H(15A)-C(15)-H(15B)	111(2)
C(12)-C(11)-H(11B)	113(2)	C(7)-C(15)-H(15C)	109.5(16)
C(4)-C(11)-H(11B)	105(2)	H(15A)-C(15)-H(15C)	104(3)
H(11A)-C(11)-H(11B)	111(3)	H(15B)-C(15)-H(15C)	108(2)
C(8)-C(12)-C(11)	106.2(2)	N(1)-C(16)-H(16A)	118.8(18)
C(8)-C(12)-H(12A)	107.0(19)	N(1)-C(16)-H(16B)	106(2)
C(11)-C(12)-H(12A)	110.9(19)	H(16A)-C(16)-H(16B)	104(2)
C(8)-C(12)-H(12B)	106.1(17)	N(1)-C(16)-H(16C)	109(2)
C(11)-C(12)-H(12B)	113.2(17)	H(16A)-C(16)-H(16C)	108(3)
H(12A)-C(12)-H(12B)	113(2)	H(16B)-C(16)-H(16C)	111(3)
C(14)-C(13)-C(5)	106.0(2)	H(5A)-O(5)-H(5B)	117(4)

Table A4.4. Anisotropic displacement parameters ($Å^2 x\ 10^4$) for RUN03 (CCDC 821739). The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$.

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	109(1)	272(2)	281(1)	-65(1)	38(1)	-28(1)
O(1)	253(12)	613(19)	192(12)	29(11)	-85(10)	-97(12)
O(2)	114(8)	342(14)	314(13)	-28(11)	11(9)	-29(8)
O(3)	157(9)	229(11)	189(9)	26(9)	-21(7)	5(9)
O(4)	160(10)	315(15)	334(12)	3(10)	88(8)	36(9)
N(1)	161(11)	186(15)	247(13)	41(11)	18(9)	18(10)
C(1)	87(12)	400(20)	230(16)	-42(15)	21(11)	1(13)
C(2)	144(14)	370(20)	268(18)	-132(15)	-8(13)	-41(14)
C(3)	142(13)	211(19)	281(16)	-68(13)	43(11)	0(12)
C(4)	142(11)	195(15)	211(14)	-37(12)	24(11)	-13(10)
C(5)	95(11)	195(14)	150(13)	-3(9)	5(10)	-6(11)
C(6)	93(12)	233(19)	172(15)	-19(13)	14(10)	41(12)
C(7)	123(13)	242(19)	142(13)	24(12)	-12(10)	18(11)
C(8)	100(11)	183(16)	142(14)	-6(12)	10(10)	26(10)
C(9)	93(10)	231(17)	146(12)	22(13)	41(9)	-17(12)
C(10)	138(10)	243(16)	191(14)	-22(14)	43(12)	21(10)
C(11)	121(12)	180(18)	268(17)	-23(14)	19(11)	31(12)
C(12)	108(12)	258(18)	173(15)	-18(12)	16(10)	19(12)
C(13)	136(12)	204(18)	161(14)	-20(13)	46(11)	13(12)
C(14)	180(14)	270(20)	214(16)	29(14)	37(11)	-3(12)
C(15)	181(14)	330(20)	159(15)	15(14)	-5(11)	-18(14)
C(16)	252(15)	240(20)	362(19)	67(15)	27(14)	18(14)
O(5)	298(12)	341(16)	210(13)	-13(11)	2(11)	106(10)

Table A4.5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for RUN03 (CCDC 821739).

	x	y	z	U_{iso}
H(4)	8310(50)	6090(30)	5680(20)	51(11)
H(2)	10340(40)	11260(20)	7496(16)	17(8)
H(3)	8440(30)	12040(20)	6632(14)	6(7)
H(6)	9290(40)	8530(20)	6709(16)	10(8)
H(9)	5160(40)	7890(20)	5518(16)	13(7)
H(10)	6110(20)	6077(14)	6215(9)	-32(3)
H(11A)	5520(40)	10830(20)	7208(15)	3(7)
H(11B)	4650(40)	11270(30)	6490(18)	27(10)
H(12A)	3500(40)	9440(20)	6959(18)	34(10)
H(12B)	3440(40)	9670(20)	6015(16)	24(8)
H(13A)	9740(50)	9080(30)	5390(19)	36(10)
H(13B)	7880(40)	8820(20)	5110(14)	9(7)
H(14A)	9380(50)	10810(30)	5064(16)	22(9)
H(14B)	7710(50)	10310(20)	4472(17)	33(8)
H(15A)	4910(50)	8260(30)	7966(19)	37(10)
H(15B)	5940(40)	9460(20)	8057(15)	12(7)
H(15C)	6790(40)	8260(20)	8268(15)	9(7)
H(16A)	7690(40)	12560(30)	5357(16)	39(9)
H(16B)	5630(50)	12360(30)	5580(20)	43(10)
H(16C)	6260(50)	12170(30)	4719(19)	39(10)
H(5A)	9120(50)	4730(30)	5900(20)	36(11)
H(5B)	9480(70)	4720(40)	5120(20)	68(16)

Table A4.6. Hydrogen bonds for RUN03 (CCDC 821739) [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(4)-H(4)...O(5)	1.14(4)	1.55(4)	2.680(3)	173(3)
O(5)-H(5A)...O(1)#1	0.79(4)	2.05(4)	2.841(3)	177(4)
O(5)-H(5B)...N(1)#2	0.86(5)	2.06(5)	2.865(3)	157(4)

Symmetry transformations used to generate equivalent atoms:
#1 -x+2,y-1/2,-z+3/2
#2 x+1/2,-y+3/2,-z+1

A4.2. Crystal Structure analysis of ketal 238.

Figure A4.2. Ketal **238**. Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition number 845603.

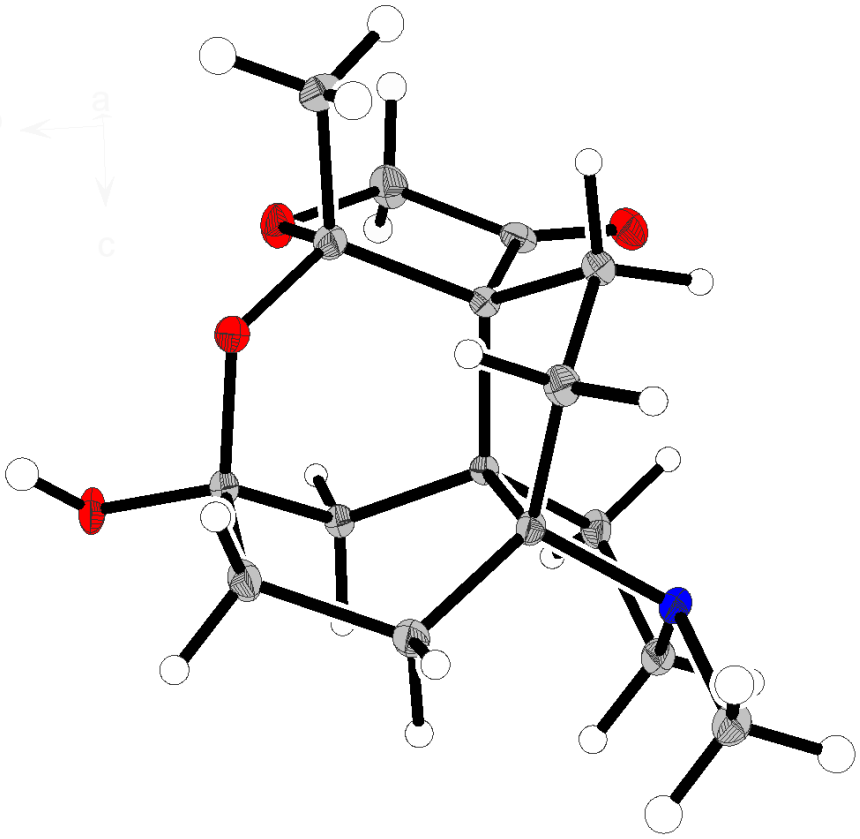
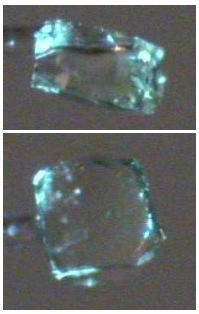


Table A4.7. Crystal data and structure refinement for ketal **238.**



Empirical formula	$C_{16}H_{23}NO_4$
Formula weight	293.35
Crystallization Solvent	Dichlromethane/iso-octane
Crystal Habit	Block
Crystal size	0.32 x 0.31 x 0.19 mm^3
Crystal color	Colorless

Data Collection

Type of diffractometer	Bruker KAPPA APEX II	
Wavelength	0.71073 Å MoKα	
Data Collection Temperature	100(2) K	
θ range for 9695 reflections used in lattice determination	2.51 to 41.09°	
Unit cell dimensions	a = 12.1329(5) Å b = 14.5974(6) Å c = 16.4163(7) Å	α= 90° β= 90° γ = 90°
Volume	2907.5(2) $Å^3$	
Z	8	
Crystal system	Orthorhombic	
Space group	$P\ 2_12_12_1$	
Density (calculated)	1.340 Mg/m^3	
F(000)	1264	
Data collection program	Bruker APEX2 v2009.7-0	
θ range for data collection	1.87 to 43.45°	
Completeness to θ = 43.45°	98.8 %	
Index ranges	$-23 \le h \le 23, -26 \le k \le 28, -30 \le l \le 31$	
Data collection scan type	ω scans; 10 settings	
Data reduction program	Bruker SAINT-Plus v7.68A	
Reflections collected	125921	
Independent reflections	21388 [R_{int}= 0.0565]	
Absorption coefficient	0.096 mm^{-1}	
Absorption correction	None	
Max. and min. transmission	0.9820 and 0.9700	

Table A4.7. (continued)

Structure solution and Refinement

Structure solution program	SHELXS-97 (Sheldrick, 2008)
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Geometric positions
Structure refinement program	SHELXL-97 (Sheldrick, 2008)
Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	21388 / 0 / 385
Treatment of hydrogen atoms	Riding
Goodness-of-fit on F^2	1.728
Final R indices [$I>2\sigma(I)$, 15751 reflections]	R1 = 0.0420, *w*R2 = 0.0639
R indices (all data)	R1 = 0.0649, *w*R2 = 0.0649
Type of weighting scheme used	Sigma
Weighting scheme used	$w=1/\sigma^2(Fo^2)$
Max shift/error	0.001
Average shift/error	0.000
Absolute structure parameter	-0.3(3)
Largest diff. peak and hole	0.496 and -0.336 e.Å^{-3}

Special Refinement Details

Crystals were mounted on a glass fiber using Paratone oil then placed on the diffractometer under a nitrogen stream at 100K.

Refinement of F^2 against ALL reflections. The weighted R-factor (*w*R) and goodness of fit (S) are based on F^2, conventional R-factors (R) are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R-factors based on ALL data will be even larger.

All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Table A4.8. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for RUN04 (CCDC 845603). U(eq) is defined as the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
O(1A)	5554(1)	2458(1)	3635(1)	17(1)
O(2A)	5617(1)	4860(1)	3573(1)	16(1)
O(3A)	6856(1)	5367(1)	4536(1)	13(1)
O(4A)	5534(1)	6195(1)	5244(1)	15(1)
N(1A)	6999(1)	2778(1)	6210(1)	12(1)
C(1A)	5743(1)	3265(1)	3721(1)	12(1)
C(2A)	5213(1)	4024(1)	3234(1)	17(1)
C(3A)	6665(1)	4676(1)	3962(1)	12(1)
C(4A)	6553(1)	3693(1)	4317(1)	10(1)
C(5A)	7642(1)	3165(1)	4411(1)	12(1)
C(6A)	8139(1)	3580(1)	5187(1)	12(1)
C(7A)	7155(1)	3664(1)	5767(1)	10(1)
C(8A)	7224(1)	4482(1)	6354(1)	12(1)
C(9A)	7050(1)	5431(1)	5965(1)	13(1)
C(10A)	6201(1)	5414(1)	5272(1)	11(1)
C(11A)	5454(1)	4596(1)	5351(1)	10(1)
C(12A)	6098(1)	3720(1)	5213(1)	8(1)
C(13A)	5397(1)	2880(1)	5456(1)	12(1)
C(14A)	5810(1)	2651(1)	6303(1)	14(1)
C(15A)	7614(1)	2662(1)	6969(1)	18(1)
C(16A)	7580(1)	4788(1)	3341(1)	18(1)
O(1B)	2680(1)	7609(1)	2857(1)	29(1)
O(2B)	2933(1)	5215(1)	2843(1)	17(1)
O(3B)	1616(1)	4626(1)	3711(1)	14(1)
O(4B)	2919(1)	3806(1)	4444(1)	14(1)
N(1B)	1310(1)	7158(1)	5459(1)	12(1)
C(1B)	2641(1)	6797(1)	2993(1)	19(1)
C(2B)	3378(1)	6081(1)	2610(1)	24(1)
C(3B)	1831(1)	5337(1)	3167(1)	15(1)
C(4B)	1832(1)	6307(1)	3550(1)	14(1)
C(5B)	708(1)	6775(1)	3641(1)	17(1)
C(6B)	225(1)	6340(1)	4408(1)	16(1)
C(7B)	1197(1)	6278(1)	4998(1)	11(1)
C(8B)	1143(1)	5441(1)	5566(1)	15(1)
C(9B)	1342(1)	4518(1)	5139(1)	16(1)
C(10B)	2228(1)	4574(1)	4473(1)	12(1)
C(11B)	2944(1)	5407(1)	4592(1)	11(1)
C(12B)	2268(1)	6268(1)	4452(1)	10(1)
C(13B)	2931(1)	7117(1)	4725(1)	13(1)
C(14B)	2492(1)	7309(1)	5570(1)	14(1)
C(15B)	686(1)	7231(1)	6218(1)	17(1)
C(16B)	1021(1)	5208(1)	2474(1)	24(1)

Table A4.9. Bond lengths [Å] and angles [°] for RUN04 (CCDC 845603).

O(1A)-C(1A)	1.2077(9)	C(2A)-O(2A)-C(3A)	108.34(5)
O(2A)-C(2A)	1.4278(9)	C(3A)-O(3A)-C(10A)	120.30(5)
O(2A)-C(3A)	1.4486(9)	C(15A)-N(1A)-C(14A)	113.62(6)
O(3A)-C(3A)	1.3986(9)	C(15A)-N(1A)-C(7A)	116.75(6)
O(3A)-C(10A)	1.4485(8)	C(14A)-N(1A)-C(7A)	106.52(5)
O(4A)-C(10A)	1.3994(9)	O(1A)-C(1A)-C(2A)	124.87(7)
N(1A)-C(15A)	1.4614(10)	O(1A)-C(1A)-C(4A)	126.79(7)
N(1A)-C(14A)	1.4631(10)	C(2A)-C(1A)-C(4A)	108.33(6)
N(1A)-C(7A)	1.4967(9)	O(2A)-C(2A)-C(1A)	105.95(6)
C(1A)-C(2A)	1.5100(11)	O(3A)-C(3A)-O(2A)	108.02(5)
C(1A)-C(4A)	1.5211(10)	O(3A)-C(3A)-C(16A)	104.69(6)
C(3A)-C(16A)	1.5170(10)	O(2A)-C(3A)-C(16A)	109.02(6)
C(3A)-C(4A)	1.5552(10)	O(3A)-C(3A)-C(4A)	115.33(6)
C(4A)-C(5A)	1.5368(10)	O(2A)-C(3A)-C(4A)	105.04(5)
C(4A)-C(12A)	1.5710(9)	C(16A)-C(3A)-C(4A)	114.53(6)
C(5A)-C(6A)	1.5331(10)	C(1A)-C(4A)-C(5A)	114.48(6)
C(6A)-C(7A)	1.5317(10)	C(1A)-C(4A)-C(3A)	101.21(5)
C(7A)-C(8A)	1.5366(10)	C(5A)-C(4A)-C(3A)	115.17(6)
C(7A)-C(12A)	1.5748(10)	C(1A)-C(4A)-C(12A)	112.67(6)
C(8A)-C(9A)	1.5409(10)	C(5A)-C(4A)-C(12A)	102.78(5)
C(9A)-C(10A)	1.5341(10)	C(3A)-C(4A)-C(12A)	110.93(6)
C(10A)-C(11A)	1.5041(10)	C(6A)-C(5A)-C(4A)	102.93(6)
C(11A)-C(12A)	1.5158(10)	C(7A)-C(6A)-C(5A)	103.98(6)
C(12A)-C(13A)	1.5453(10)	N(1A)-C(7A)-C(6A)	109.33(6)
C(13A)-C(14A)	1.5139(11)	N(1A)-C(7A)-C(8A)	111.91(5)
O(1B)-C(1B)	1.2068(10)	C(6A)-C(7A)-C(8A)	114.21(6)
O(2B)-C(2B)	1.4270(10)	N(1A)-C(7A)-C(12A)	102.88(5)
O(2B)-C(3B)	1.4499(9)	C(6A)-C(7A)-C(12A)	106.25(5)
O(3B)-C(3B)	1.3948(9)	C(8A)-C(7A)-C(12A)	111.51(6)
O(3B)-C(10B)	1.4555(8)	C(7A)-C(8A)-C(9A)	115.50(6)
O(4B)-C(10B)	1.4001(9)	C(10A)-C(9A)-C(8A)	112.63(6)
N(1B)-C(14B)	1.4623(10)	O(4A)-C(10A)-O(3A)	109.19(6)
N(1B)-C(15B)	1.4625(10)	O(4A)-C(10A)-C(11A)	107.44(5)
N(1B)-C(7B)	1.4965(10)	O(3A)-C(10A)-C(11A)	111.42(6)
C(1B)-C(2B)	1.5122(12)	O(4A)-C(10A)-C(9A)	113.55(6)
C(1B)-C(4B)	1.5198(11)	O(3A)-C(10A)-C(9A)	104.54(5)
C(3B)-C(16B)	1.5152(11)	C(11A)-C(10A)-C(9A)	110.74(6)
C(3B)-C(4B)	1.5493(11)	C(10A)-C(11A)-C(12A)	110.20(5)
C(4B)-C(5B)	1.5329(10)	C(11A)-C(12A)-C(13A)	110.34(6)
C(4B)-C(12B)	1.5728(10)	C(11A)-C(12A)-C(4A)	110.08(6)
C(5B)-C(6B)	1.5285(12)	C(13A)-C(12A)-C(4A)	114.53(6)
C(6B)-C(7B)	1.5291(10)	C(11A)-C(12A)-C(7A)	112.16(6)
C(7B)-C(8B)	1.5371(11)	C(13A)-C(12A)-C(7A)	104.90(5)
C(7B)-C(12B)	1.5795(10)	C(4A)-C(12A)-C(7A)	104.63(5)
C(8B)-C(9B)	1.5383(11)	C(14A)-C(13A)-C(12A)	103.35(6)
C(9B)-C(10B)	1.5349(10)	N(1A)-C(14A)-C(13A)	101.71(6)
C(10B)-C(11B)	1.5077(10)	C(2B)-O(2B)-C(3B)	109.79(6)
C(11B)-C(12B)	1.5181(10)	C(3B)-O(3B)-C(10B)	119.57(5)
C(12B)-C(13B)	1.5440(10)	C(14B)-N(1B)-C(15B)	112.94(6)
C(13B)-C(14B)	1.5123(11)	C(14B)-N(1B)-C(7B)	106.39(6)
		C(15B)-N(1B)-C(7B)	116.48(6)

O(1B)-C(1B)-C(2B)	125.30(8)	N(1B)-C(7B)-C(12B)	102.70(6)
O(1B)-C(1B)-C(4B)	126.79(8)	C(6B)-C(7B)-C(12B)	105.98(5)
C(2B)-C(1B)-C(4B)	107.88(7)	C(8B)-C(7B)-C(12B)	111.83(6)
O(2B)-C(2B)-C(1B)	106.06(7)	C(7B)-C(8B)-C(9B)	114.43(6)
O(3B)-C(3B)-O(2B)	108.45(6)	C(10B)-C(9B)-C(8B)	112.82(6)
O(3B)-C(3B)-C(16B)	105.52(6)	O(4B)-C(10B)-O(3B)	108.59(6)
O(2B)-C(3B)-C(16B)	107.94(6)	O(4B)-C(10B)-C(11B)	107.73(5)
O(3B)-C(3B)-C(4B)	114.84(6)	O(3B)-C(10B)-C(11B)	111.32(6)
O(2B)-C(3B)-C(4B)	105.07(6)	O(4B)-C(10B)-C(9B)	113.59(6)
C(16B)-C(3B)-C(4B)	114.75(6)	O(3B)-C(10B)-C(9B)	104.90(5)
C(1B)-C(4B)-C(5B)	115.01(7)	C(11B)-C(10B)-C(9B)	110.73(6)
C(1B)-C(4B)-C(3B)	100.74(6)	C(10B)-C(11B)-C(12B)	109.66(5)
C(5B)-C(4B)-C(3B)	116.50(6)	C(11B)-C(12B)-C(13B)	109.81(6)
C(1B)-C(4B)-C(12B)	111.49(6)	C(11B)-C(12B)-C(4B)	110.76(6)
C(5B)-C(4B)-C(12B)	102.93(6)	C(13B)-C(12B)-C(4B)	114.82(6)
C(3B)-C(4B)-C(12B)	110.44(6)	C(11B)-C(12B)-C(7B)	111.47(6)
C(6B)-C(5B)-C(4B)	103.66(6)	C(13B)-C(12B)-C(7B)	104.82(6)
C(5B)-C(6B)-C(7B)	104.52(6)	C(4B)-C(12B)-C(7B)	104.94(5)
N(1B)-C(7B)-C(6B)	109.86(6)	C(14B)-C(13B)-C(12B)	103.41(6)
N(1B)-C(7B)-C(8B)	112.33(6)	N(1B)-C(14B)-C(13B)	101.70(6)
C(6B)-C(7B)-C(8B)	113.44(6)		

Table A4.10. Anisotropic displacement parameters ($Å^2 x\ 10^4$) for RUN04 (CCDC 845603). The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$.

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1A)	216(3)	132(3)	168(3)	-42(2)	-12(2)	-11(2)
O(2A)	200(3)	117(2)	152(2)	0(2)	-63(2)	22(2)
O(3A)	158(2)	98(2)	123(2)	-3(2)	16(2)	-17(2)
O(4A)	155(3)	68(2)	213(3)	19(2)	14(2)	16(2)
N(1A)	156(3)	98(3)	101(3)	17(2)	-12(2)	13(2)
C(1A)	131(3)	137(3)	96(3)	-24(3)	13(3)	12(3)
C(2A)	214(4)	152(4)	148(3)	-30(3)	-62(3)	16(3)
C(3A)	153(3)	102(3)	97(3)	3(3)	-10(2)	7(3)
C(4A)	122(3)	86(3)	89(3)	-5(3)	11(2)	3(3)
C(5A)	125(3)	106(3)	119(3)	-1(3)	20(3)	24(3)
C(6A)	113(3)	116(3)	138(3)	-4(3)	-6(3)	16(3)
C(7A)	120(3)	78(3)	95(3)	8(2)	-11(2)	11(3)
C(8A)	155(3)	109(3)	105(3)	-9(3)	-19(3)	8(3)
C(9A)	179(3)	90(3)	133(3)	-19(3)	-18(3)	2(3)
C(10A)	140(3)	79(3)	111(3)	4(3)	17(2)	21(3)
C(11A)	113(3)	87(3)	107(3)	2(3)	9(2)	11(3)
C(12A)	91(3)	77(3)	85(3)	1(3)	5(2)	1(2)
C(13A)	112(3)	84(3)	157(3)	5(3)	15(3)	-4(2)
C(14A)	172(4)	107(3)	142(3)	19(3)	43(3)	8(3)
C(15A)	259(4)	143(4)	127(3)	12(3)	-40(3)	50(3)
C(16A)	248(4)	157(4)	135(3)	22(3)	50(3)	-14(3)
O(1B)	519(4)	124(3)	222(3)	45(2)	109(3)	30(3)
O(2B)	238(3)	116(3)	164(2)	-1(2)	44(2)	26(2)
O(3B)	165(2)	99(2)	152(2)	-7(2)	-46(2)	-8(2)
O(4B)	157(2)	69(2)	200(3)	-13(2)	-25(2)	12(2)
N(1B)	128(3)	105(3)	121(3)	-23(2)	3(2)	9(2)
C(1B)	320(5)	131(4)	119(3)	8(3)	27(3)	18(3)
C(2B)	359(5)	136(4)	219(4)	21(3)	98(4)	4(3)
C(3B)	188(4)	115(3)	133(3)	-12(3)	-26(3)	35(3)
C(4B)	185(4)	98(3)	125(3)	12(3)	-19(3)	31(3)
C(5B)	216(4)	144(4)	164(4)	-28(3)	-74(3)	76(3)
C(6B)	123(3)	162(4)	208(4)	-53(3)	-38(3)	31(3)
C(7B)	110(3)	88(3)	133(3)	-9(3)	1(3)	7(3)
C(8B)	160(3)	119(3)	163(3)	10(3)	32(3)	0(3)
C(9B)	186(4)	100(3)	193(4)	16(3)	25(3)	-12(3)
C(10B)	132(3)	78(3)	138(3)	7(3)	-24(3)	8(3)
C(11B)	110(3)	86(3)	127(3)	6(3)	-7(2)	9(3)
C(12B)	106(3)	72(3)	116(3)	4(3)	1(2)	1(3)
C(13B)	132(3)	89(3)	176(3)	0(3)	8(3)	-7(3)
C(14B)	153(4)	113(3)	164(4)	-23(3)	-26(3)	-8(3)
C(15B)	198(4)	169(4)	147(4)	-13(3)	24(3)	28(3)
C(16B)	327(5)	203(4)	181(4)	-43(3)	-97(3)	70(4)

Table A4.11. Hydrogen bonds for RUN04 (CCDC 845603) [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(4A)-H(4A)...N(1B)#1	0.84	2.02	2.8290(8)	160.1
O(4B)-H(4B)...N(1A)#2	0.84	1.96	2.7835(8)	166.4

Symmetry transformations used to generate equivalent atoms:
#1 x+1/2,-y+3/2,-z+1
#2 x-1/2,-y+1/2,-z+1

A4.3. Crystal Structure analysis of hexacycle 255.

Figure A4.2. Hexacycle **255**.

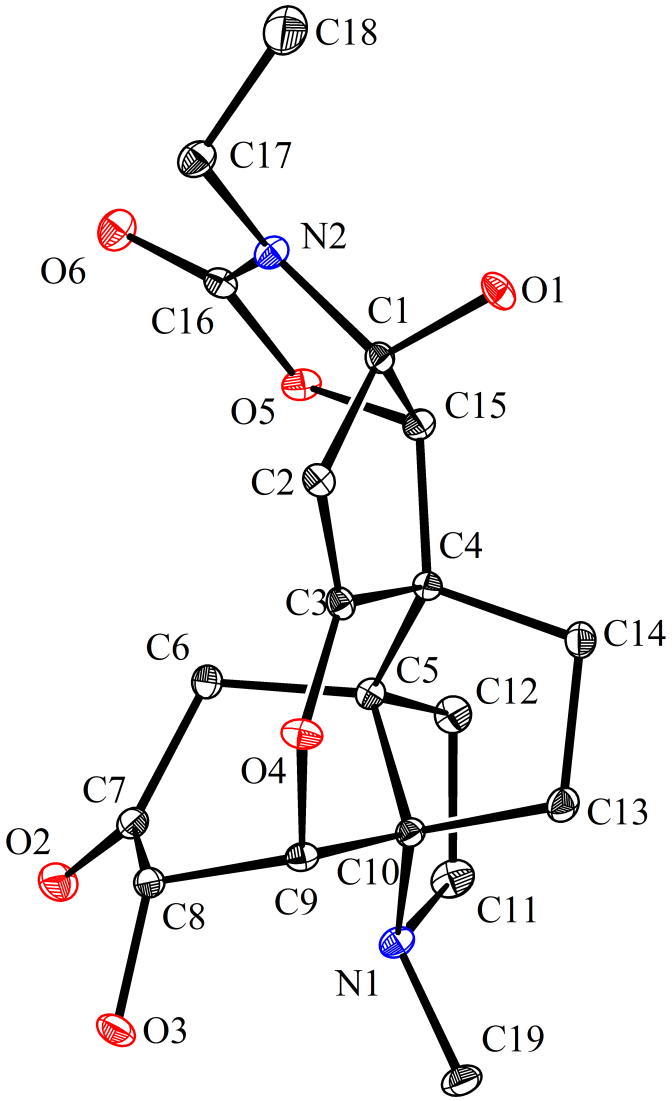


Table A4.12. Crystal Data and Structure Analysis Details for hexacycle **255.**

Empirical formula	C20 H25 Cl3 N2 O6
Formula weight	495.77
Crystallization solvent	chloroform
Crystal shape	blade
Crystal color	colourless
Crystal size	0.07 x 0.10 x 0.38 mm

Data Collection

Preliminary photograph(s)	rotation	
Type of diffractometer	Bruker APEX-II CCD	
Wavelength	0.71073 Å MoK	
Data collection temperature	100 K	
Theta range for 9903 reflections used in lattice determination	2.37 to 34.99°	
Unit cell dimensions	a = 6.7127(3) Å b = 14.4750(7) Å c = 10.7522(6) Å	a= 90° b= 95.003(3)° g = 90°
Volume	1040.77(9) $Å^3$	
Z	2	
Crystal system	monoclinic	
Space group	P 1 21 1 (# 4)	
Density (calculated)	1.582 g/cm^3	
F(000)	516	
Theta range for data collection	1.9 to 37.1°	
Completeness to theta = 25.000°	99.9%	
Index ranges	-10 £ h £ 11, -24 £ k £ 24, -17 £ l £ 17	
Data collection scan type	and scans	
Reflections collected	42130	
Independent reflections	9868 [R_{int}= 0.0488]	
Reflections > 2s(I)	8802	
Average s(I)/(net I)	0.0474	
Absorption coefficient	0.48 mm^{-1}	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.0000 and 0.9024	

Table A4.12. (continued)

Structure Solution and Refinement

Primary solution method	dual
Secondary solution method	?
Hydrogen placement	difmap
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	9868 / 1 / 380
Treatment of hydrogen atoms	refall
Goodness-of-fit on F^2	1.20
Final R indices [I>2s(I), 8802 reflections]	R1 = 0.0370, wR2 = 0.0744
R indices (all data)	R1 = 0.0459, wR2 = 0.0770
Type of weighting scheme used	calc
Weighting scheme used	w=1/[^2^(Fo^2^)+(0.0300P)^2^] where P=(Fo^2^+2Fc^2^)/3
Max shift/error	0.001
Average shift/error	0.000
Absolute structure parameter	0.046(15)
Extinction coefficient	n/a
Largest diff. peak and hole	0.51 and -0.27 e·Å^{-3}

Programs Used

Cell refinement	SAINT V8.32B (Bruker-AXS, 2007)
Data collection	APEX2 2013.2-0 (Bruker-AXS, 2007)
Data reduction	SAINT V8.32B (Bruker-AXS, 2007)
Structure solution	SHELXT (Sheldrick, 2012)
Structure refinement	SHELXL-2013/2 (Sheldrick, 2013)
Graphics	DIAMOND 3 (Crystal Impact, 1999)

References

Special Refinement Details

Table A4.13. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for run08. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
O(1)	5492(2)	10893(1)	6327(1)	11(1)
O(2)	-1017(2)	7011(1)	8955(1)	14(1)
O(3)	2649(2)	6411(1)	9950(1)	13(1)
O(4)	5085(2)	8311(1)	8663(1)	10(1)
O(5)	691(2)	10026(1)	6578(1)	10(1)
O(6)	-791(2)	11151(1)	7604(1)	13(1)
N(1)	2162(2)	6446(1)	6944(2)	9(1)
N(2)	2603(2)	11166(1)	7397(1)	9(1)
C(1)	4063(2)	10485(1)	7032(2)	8(1)
C(2)	4938(2)	9904(1)	8105(2)	8(1)
C(3)	4478(2)	9016(1)	7889(2)	8(1)
C(4)	3356(2)	8845(1)	6616(2)	7(1)
C(5)	1859(2)	8058(1)	6755(2)	8(1)
C(6)	416(2)	8230(1)	7782(2)	9(1)
C(7)	441(2)	7447(1)	8698(2)	9(1)
C(8)	2499(2)	7289(1)	9377(2)	9(1)
C(9)	4159(2)	7404(1)	8484(2)	8(1)
C(10)	3376(2)	7282(1)	7116(2)	8(1)
C(11)	783(3)	6592(1)	5813(2)	13(1)
C(12)	728(2)	7644(1)	5571(2)	11(1)
C(13)	5071(2)	7415(1)	6236(2)	10(1)
C(14)	4881(2)	8425(1)	5776(2)	10(1)
C(15)	2689(2)	9817(1)	6235(2)	8(1)
C(16)	735(2)	10824(1)	7238(2)	9(1)
C(17)	3148(3)	11961(1)	8193(2)	12(1)
C(18)	3986(4)	12748(2)	7479(3)	29(1)
C(19)	3298(3)	5585(1)	6923(2)	13(1)
Cl(1)	2513(1)	9965(1)	10419(1)	18(1)
Cl(2)	1398(1)	9278(1)	12784(1)	25(1)
Cl(3)	-1371(1)	9156(1)	10564(1)	16(1)
C(20)	527(3)	9823(1)	11365(2)	12(1)

Table A4.14. Bond lengths [Å] and angles [°] for hexacycle **253**.

O(1)-H(1)	0.87(3)
O(1)-C(1)	1.403(2)
O(2)-C(7)	1.216(2)
O(3)-H(3)	0.84(3)
O(3)-C(8)	1.412(2)
O(4)-C(3)	1.357(2)
O(4)-C(9)	1.459(2)
O(5)-C(15)	1.4535(19)
O(5)-C(16)	1.355(2)
O(6)-C(16)	1.223(2)
N(1)-C(10)	1.462(2)
N(1)-C(11)	1.478(2)
N(1)-C(19)	1.462(2)
N(2)-C(1)	1.467(2)
N(2)-C(16)	1.346(2)
N(2)-C(17)	1.462(2)
C(1)-C(2)	1.505(2)
C(1)-C(15)	1.544(2)
C(2)-H(2)	0.96(3)
C(2)-C(3)	1.338(2)
C(3)-C(4)	1.524(2)
C(4)-C(5)	1.535(2)
C(4)-C(14)	1.547(2)
C(4)-C(15)	1.523(2)
C(5)-C(6)	1.551(2)
C(5)-C(10)	1.543(2)
C(5)-C(12)	1.545(2)
C(6)-H(6A)	0.92(3)
C(6)-H(6B)	0.97(3)
C(6)-C(7)	1.501(2)
C(7)-C(8)	1.523(2)
C(8)-H(8)	0.92(3)
C(8)-C(9)	1.542(2)
C(9)-H(9)	0.94(2)
C(9)-C(10)	1.528(2)
C(10)-C(13)	1.554(2)
C(11)-H(11A)	0.98(3)
C(11)-H(11B)	0.95(2)
C(11)-C(12)	1.544(2)
C(12)-H(12A)	0.96(3)
C(12)-H(12B)	0.89(2)
C(13)-H(13A)	0.90(3)
C(13)-H(13B)	0.92(2)
C(13)-C(14)	1.544(2)
C(14)-H(14A)	0.96(3)
C(14)-H(14B)	0.92(2)
C(15)-H(15)	1.00(2)
C(17)-H(17A)	0.91(3)
C(17)-H(17B)	0.95(2)
C(17)-C(18)	1.509(3)
C(18)-H(18A)	0.89(4)

C(18)-H(18B)	0.97(3)
C(18)-H(18C)	1.01(5)
C(19)-H(19A)	1.00(3)
C(19)-H(19B)	0.91(3)
C(19)-H(19C)	0.97(3)
Cl(1)-C(20)	1.7580(18)
Cl(2)-C(20)	1.7706(19)
Cl(3)-C(20)	1.7626(19)
C(20)-H(20)	0.88(3)

C(1)-O(1)-H(1)	105.7(19)
C(8)-O(3)-H(3)	108(2)
C(3)-O(4)-C(9)	119.62(13)
C(16)-O(5)-C(15)	109.38(12)
C(10)-N(1)-C(11)	106.73(13)
C(10)-N(1)-C(19)	114.96(13)
C(19)-N(1)-C(11)	113.54(14)
C(16)-N(2)-C(1)	110.85(14)
C(16)-N(2)-C(17)	123.14(14)
C(17)-N(2)-C(1)	123.15(13)
O(1)-C(1)-N(2)	111.46(13)
O(1)-C(1)-C(2)	114.21(13)
O(1)-C(1)-C(15)	111.52(14)
N(2)-C(1)-C(2)	113.29(14)
N(2)-C(1)-C(15)	100.87(12)
C(2)-C(1)-C(15)	104.46(13)
C(1)-C(2)-H(2)	123.4(15)
C(3)-C(2)-C(1)	109.59(15)
C(3)-C(2)-H(2)	127.0(15)
O(4)-C(3)-C(4)	121.84(14)
C(2)-C(3)-O(4)	124.29(16)
C(2)-C(3)-C(4)	113.64(14)
C(3)-C(4)-C(5)	108.04(13)
C(3)-C(4)-C(14)	106.72(12)
C(5)-C(4)-C(14)	103.76(13)
C(15)-C(4)-C(3)	101.67(13)
C(15)-C(4)-C(5)	122.16(12)
C(15)-C(4)-C(14)	113.59(14)
C(4)-C(5)-C(6)	113.87(13)
C(4)-C(5)-C(10)	98.11(12)
C(4)-C(5)-C(12)	119.09(14)
C(10)-C(5)-C(6)	112.16(14)
C(10)-C(5)-C(12)	101.03(13)
C(12)-C(5)-C(6)	110.91(13)
C(5)-C(6)-H(6A)	110.2(15)
C(5)-C(6)-H(6B)	109.2(15)
H(6A)-C(6)-H(6B)	105(2)
C(7)-C(6)-C(5)	111.92(13)
C(7)-C(6)-H(6A)	107.0(16)
C(7)-C(6)-H(6B)	113.1(15)
O(2)-C(7)-C(6)	125.29(15)
O(2)-C(7)-C(8)	121.84(16)
C(6)-C(7)-C(8)	112.70(14)
O(3)-C(8)-C(7)	111.83(13)

O(3)-C(8)-H(8)	108.8(16)
O(3)-C(8)-C(9)	109.91(13)
C(7)-C(8)-H(8)	107.7(15)
C(7)-C(8)-C(9)	111.12(14)
C(9)-C(8)-H(8)	107.4(14)
O(4)-C(9)-C(8)	109.72(13)
O(4)-C(9)-H(9)	104.8(14)
O(4)-C(9)-C(10)	109.74(13)
C(8)-C(9)-H(9)	106.4(14)
C(10)-C(9)-C(8)	112.32(13)
C(10)-C(9)-H(9)	113.5(15)
N(1)-C(10)-C(5)	102.84(12)
N(1)-C(10)-C(9)	111.01(13)
N(1)-C(10)-C(13)	117.09(14)
C(5)-C(10)-C(13)	104.98(13)
C(9)-C(10)-C(5)	108.84(13)
C(9)-C(10)-C(13)	111.27(13)
N(1)-C(11)-H(11A)	103.4(18)
N(1)-C(11)-H(11B)	114.0(15)
N(1)-C(11)-C(12)	106.48(13)
H(11A)-C(11)-H(11B)	106(2)
C(12)-C(11)-H(11A)	115.2(17)
C(12)-C(11)-H(11B)	111.5(15)
C(5)-C(12)-H(12A)	111.4(15)
C(5)-C(12)-H(12B)	109.2(16)
C(11)-C(12)-C(5)	103.93(14)
C(11)-C(12)-H(12A)	110.8(15)
C(11)-C(12)-H(12B)	112.3(16)
H(12A)-C(12)-H(12B)	109(2)
C(10)-C(13)-H(13A)	108.3(18)
C(10)-C(13)-H(13B)	112.3(15)
H(13A)-C(13)-H(13B)	106(2)
C(14)-C(13)-C(10)	105.56(13)
C(14)-C(13)-H(13A)	112.7(18)
C(14)-C(13)-H(13B)	112.3(16)
C(4)-C(14)-H(14A)	111.1(15)
C(4)-C(14)-H(14B)	110.0(15)
C(13)-C(14)-C(4)	103.00(13)
C(13)-C(14)-H(14A)	113.6(16)
C(13)-C(14)-H(14B)	116.4(15)
H(14A)-C(14)-H(14B)	103(2)
O(5)-C(15)-C(1)	104.40(13)
O(5)-C(15)-C(4)	112.34(13)
O(5)-C(15)-H(15)	110.7(13)
C(1)-C(15)-H(15)	110.1(14)
C(4)-C(15)-C(1)	106.38(13)
C(4)-C(15)-H(15)	112.5(15)
O(6)-C(16)-O(5)	121.13(15)
O(6)-C(16)-N(2)	127.91(16)
N(2)-C(16)-O(5)	110.95(14)
N(2)-C(17)-H(17A)	110(2)
N(2)-C(17)-H(17B)	107.1(16)
N(2)-C(17)-C(18)	112.43(17)
H(17A)-C(17)-H(17B)	104(3)

C(18)-C(17)-H(17A)	110(2)
C(18)-C(17)-H(17B)	112.2(15)
C(17)-C(18)-H(18A)	112(2)
C(17)-C(18)-H(18B)	108.9(19)
C(17)-C(18)-H(18C)	109(3)
H(18A)-C(18)-H(18B)	117(3)
H(18A)-C(18)-H(18C)	104(3)
H(18B)-C(18)-H(18C)	105(3)
N(1)-C(19)-H(19A)	112.3(15)
N(1)-C(19)-H(19B)	108.8(16)
N(1)-C(19)-H(19C)	108.5(15)
H(19A)-C(19)-H(19B)	107(2)
H(19A)-C(19)-H(19C)	109(2)
H(19B)-C(19)-H(19C)	111(2)
Cl(1)-C(20)-Cl(2)	109.88(9)
Cl(1)-C(20)-Cl(3)	109.45(10)
Cl(1)-C(20)-H(20)	107.4(17)
Cl(2)-C(20)-H(20)	107.8(18)
Cl(3)-C(20)-Cl(2)	110.31(10)
Cl(3)-C(20)-H(20)	111.9(16)

Table A4.15. Anisotropic displacement parameters ($Å^2 x\ 10^4$) for run08. The anisotropic displacement factor exponent takes the form: $-2p^2 [h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$.

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	77(5)	134(5)	118(6)	35(5)	29(4)	-23(4)
O(2)	111(5)	131(6)	177(7)	24(5)	43(5)	-12(4)
O(3)	132(5)	119(5)	131(6)	60(5)	23(5)	16(4)
O(4)	112(5)	76(5)	103(6)	4(4)	-36(4)	-22(4)
O(5)	68(4)	86(5)	132(6)	3(4)	-13(4)	2(4)
O(6)	79(5)	148(6)	156(7)	-13(5)	15(4)	7(4)
N(1)	88(5)	73(6)	107(7)	-21(5)	-2(5)	-6(4)
N(2)	77(5)	82(6)	110(7)	-19(5)	2(5)	-9(4)
C(1)	75(6)	83(6)	87(7)	1(5)	18(5)	-7(5)
C(2)	66(5)	99(6)	84(7)	6(6)	-4(5)	-9(5)
C(3)	62(5)	101(7)	79(7)	9(5)	11(5)	-2(5)
C(4)	68(5)	72(6)	66(7)	0(5)	-2(5)	-2(5)
C(5)	71(6)	80(6)	77(7)	-9(5)	1(5)	-3(5)
C(6)	76(6)	98(6)	90(7)	-4(5)	9(5)	-1(5)
C(7)	93(6)	83(6)	95(7)	-7(5)	12(5)	10(5)
C(8)	109(6)	81(6)	73(7)	-1(5)	4(5)	7(5)
C(9)	80(6)	69(6)	99(7)	-2(5)	1(5)	-1(5)
C(10)	75(6)	70(6)	84(7)	-6(5)	11(5)	-1(5)
C(11)	130(6)	113(7)	133(9)	-33(6)	-29(6)	-14(6)
C(12)	106(6)	123(7)	82(8)	-12(6)	-27(6)	-1(5)
C(13)	82(6)	104(7)	124(8)	-7(6)	28(5)	5(5)
C(14)	104(6)	115(7)	97(8)	-4(6)	26(5)	0(5)
C(15)	70(5)	85(6)	95(7)	-3(5)	3(5)	5(5)
C(16)	97(6)	87(6)	86(7)	17(5)	3(5)	0(5)
C(17)	122(7)	101(7)	134(8)	-27(6)	8(6)	-9(5)
C(18)	425(13)	123(8)	348(14)	-77(9)	235(12)	-107(9)
C(19)	151(7)	74(7)	176(9)	-11(6)	34(6)	14(5)
Cl(1)	179(2)	181(2)	200(2)	-37(2)	87(2)	-28(2)
Cl(2)	263(2)	343(3)	134(2)	53(2)	-6(2)	119(2)
Cl(3)	167(2)	154(2)	171(2)	-22(2)	25(2)	-30(2)
C(20)	142(7)	120(7)	112(8)	-5(6)	20(6)	19(6)

Table A4.16. Hydrogen coordinates (x 10^3) and isotropic displacement parameters (Å^{2}x 10^3) for hexacycle **253**.

	x	y	z	U_{iso}
H(1)	658(4)	1093(2)	683(3)	22(7)
H(3)	176(4)	638(2)	1046(3)	26(7)
H(2)	565(4)	1016(2)	884(2)	12(6)
H(6A)	79(4)	875(2)	823(2)	13(6)
H(6B)	-91(4)	836(2)	739(2)	14(6)
H(8)	270(3)	774(2)	998(2)	7(5)
H(9)	517(3)	698(2)	875(2)	5(5)
H(11A)	-47(4)	632(2)	604(3)	28(8)
H(11B)	114(3)	626(2)	510(2)	8(5)
H(12A)	138(4)	779(2)	483(3)	12(6)
H(12B)	-51(4)	786(2)	549(2)	11(6)
H(13A)	625(4)	730(2)	667(3)	21(7)
H(13B)	499(3)	700(2)	559(2)	8(5)
H(14A)	442(4)	848(2)	491(3)	16(6)
H(14B)	604(3)	877(2)	584(2)	10(6)
H(15)	279(3)	994(2)	532(2)	10(5)
H(17A)	404(5)	1179(2)	884(3)	32(8)
H(17B)	199(3)	1214(2)	858(2)	9(5)
H(18A)	494(5)	1256(2)	701(3)	39(9)
H(18B)	430(5)	1326(2)	805(3)	32(8)
H(18C)	291(7)	1300(4)	686(5)	85(16)
H(19A)	422(4)	558(2)	624(3)	17(6)
H(19B)	243(3)	511(2)	678(2)	14(6)
H(19C)	408(4)	552(2)	772(3)	11(6)
H(20)	10(4)	1038(2)	1155(3)	13(6)

Table A4.17. Hydrogen bonds for run08 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1)...O(6)#1	0.87(3)	1.91(3)	2.7662(18)	167(3)
O(3)-H(3)...O(6)#2	0.84(3)	2.26(3)	3.031(2)	152(3)
C(2)-H(2)...O(3)#3	0.96(3)	2.46(3)	3.341(2)	153(2)
C(2)-H(2)...Cl(3)#1	0.96(3)	2.98(2)	3.6276(17)	125.9(18)
C(9)-H(9)...O(2)#1	0.94(2)	2.55(2)	3.283(2)	135.2(18)
C(13)-H(13B)...O(1)#4	0.92(2)	2.61(3)	3.523(2)	176(2)
C(15)-H(15)...Cl(2)#5	1.00(2)	2.97(2)	3.8169(18)	143.1(18)
C(17)-H(17A)...O(3)#3	0.91(3)	2.54(3)	3.406(2)	159(3)
C(18)-H(18A)...O(1)	0.89(4)	2.56(4)	3.160(3)	125(3)
C(18)-H(18B)...Cl(3)#6	0.97(3)	2.88(3)	3.508(2)	123(2)
C(19)-H(19B)...Cl(2)#2	0.91(3)	2.91(2)	3.7129(18)	148(2)
C(20)-H(20)...O(2)#6	0.88(3)	2.52(3)	3.206(2)	136(2)

Symmetry transformations used to generate equivalent atoms:
#1 x+1,y,z #2 -x,y-1/2,-z+2 #3 -x+1,y+1/2,-z+2
#4 -x+1,y-1/2,-z+1 #5 x,y,z-1 #6 -x,y+1/2,-z+2

ABOUT THE AUTHOR

Raul Navarro was born on May 22, 1986, in Los Angeles, California to Raul Navarro Sr. and Lina Navarro. He grew up in several suburbs of the greater Los Angeles area before moving to Baldwin Park, CA at the age of six, where his parents currently reside. Raul attended Baldwin Park High School, where he ran for the cross country and track teams, and was heavily involved with several student organizations.

Raul decided to leave sunny southern California to attend Yale University in New Haven, Connecticut. While he quickly learned of the harsh winters in New England, it was during this time that Raul also discovered his passion for chemistry. The summer after his freshman year, he had the opportunity to conduct research in the laboratory of Professor John F. Hartwig. After taking organic chemistry the following school year, he decided to conduct research in the lab of Professor Glenn C. Micalizio, where he investigated polyketide synthesis and a titanium-mediated cross-coupling reaction to prepare allylic amines. It was this research experience that inspired Raul to apply to graduate school and pursue a career in academia.

Upon obtaining his bachelor's degree in 2008, Raul decided to come back to Southern California to conduct doctoral research in the lab of Professor Sarah E. Reisman at the California Institute of Technology. As an NIH predoctoral fellow, his graduate work focused on the development of new synthetic strategies for the synthesis of aza-propellane natural products. In January 2014, Raul will commence an NSF postdoctoral fellowship with Professor Thomas J. Wandless in the Chemical and Systems Biology Department at Stanford University, where he hopes to broaden his knowledge of organic chemistry through its applications in biological systems.